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Symposium on Tumors of the Hands and Feet

SYMPOSIUM: TUMORS OF THE HANDS AND FEET

INTRODUCTION

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GENERAL CONSIDERATIONS

EARLY Diagnosis.—Perhaps no regions or organs in the body are so readily favored for the early detection of tumors as are the hands and feet. Constantly under inspection, always sensitive to pain, irritation, swelling, and impairment of function, it would seem that no tumor could grow for long without early detection by the patient. Such extreme end results as the mutilation or amputation of an extremity or ultimate loss of life are the results not only of the inherent tendencies of some of these malignant tumors but more important still are often due to two avoidable losses of time. The culpability for failure to treat early tumors of the hands and feet falls either on the patient or first physician consulted, depending respectively on the time elapsing between the first recognized appearance of the tumor and the first visit to a physician, and the second period occurring between the first medical consultation and the institution of proper treatment.

Multicentric Origin.—Surgeons and pathologists are cognizant of the origin of some tumors, usually benign, in multiple foci of origin in the same organ; e.g., leiomyomas of uterus, gastrointestinal polyposis, generalized neurofibromatosis, intraductal and intracystic papillomas, and papillary carcinomas of the breast. This tendency is decidedly not common for the various regional locations of neoplasms, excluding the hands and feet, where it seems to be the rule rather than the exception. The explanation of this multicentricity is difficult to analyze because so many factors are involved. The congenital origin of some

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of these tumors seems established; for instance, multiple enchondromas, endothelial myeloma, pigmented naevi, and melanomas. In other cases a precancerosis, common to both hands, exists which later changes to multiple epitheliomas. Epitheliomas of the dorsum of the hands are often multiple and bilateral; they may appear simultaneously or at different times if the underlying precancerous state is permitted to exist or is not constantly observed. Xanthomas or giant cell tumors of tendon sheath may be single or multiple; the basic cause here may be inflammatory, as there is histologic evidence suggesting that the process merges from an inflammatory to a neoplastic hyperplasia. The idiopathic multiple hemorrhagic sarcoma of Kaposi develops bilaterally and usually concurrently on the feet and ankles of Slavic and Southern European males, who have a common physical habitus; namely, flat-feet, short sturdy legs, thick ankles, tight inelastic skin, and coexistent or antecedent circulatory disturbances of the lower extremities, such as varicosities and edema. It is inconceivable that the Kaposi tumor on one foot is a crossed metastasis from the tumor of the opposite foot, as in the beginning there is no evidence of intervening disease. Hence in Kaposi's disease there is the classical example of malignant tumors occurring multicentrically and in similar tissues, yet at such distances from each other as to defy any explanation other than the existence of a common predisposing state. At the onset the first lesions may resemble infection, but this is probably not the true mode of genesis for two reasons. Our attempts at excision and inoculation of the same patient with filtrates and macerated tumor tissue have been unsuccessful in transplanting this tumor. The disease evolutes through three stages: an inflammatory macule, a granulomatous papule or nodule, and finally a true confluent neoplasm, of varied and complex structures, composed of the tissue elements (nerve, connective tissue, smooth muscle, endothelium) found in the intricate neurovascular annexes; hardly the simple form of tumor one would expect to develop from infection or inflammation.

Precancerous Lesions.—In the entire field of cancer prophylaxis no greater opportunity exists than in the case of epitheliomas of the hands and feet. It is not an exaggeration to say that practically all of them could be prevented. The abuse or excessive use of arsenical medication, excessive exposure to sunlight for many years, occupational dermatitis of the hands in workers with tar and oil products, the chronic irradiation of the hands of physicians and technicians employing x-rays and radium, improper early treatment of burns by failure to skin graft, and other causes contributory to scarring of the skin are uniformly preventable. It may require twenty or thirty years of such chronic irritation to induce these precancerous lesions of the skin, so that prophylaxis should be applied in early life and not delayed until later when the effects begin to be manifested. Once the pre-

cancerous changes in the skin are apparent, i.e., atrophy, hyperkeratosis, loss of oil and sweat glands, much can be done by careful hygiene of the hands. Keratoses may be treated by electrodesiccation or by beta irradiation (Fig. 12). Bland vegetable oils or animal fats should be applied to the dry skin. One precancerous state which cannot be prevented and which seems chiefly to involve the hands and feet is the so-called acrodermatitis chronica atrophicans. This disease is somewhat similar to scleroderma; the skin of the hands and feet, later of the forearms and legs, undergoes spontaneous progressive atrophy. The

Fig. 1.—Spindle-cell epidermoid carcinoma developing in acrodermatitis chronica atrophicans. This precancerous disease is more marked on the left hand. Note the atrophy, transparency, and anetodermia.

skin becomes thin, violaceous, and transparent. The oil and sweat glands disappear, together with the elastic tissue. (Fig. 1.) In time epitheliomas, often multiple, develop and may metastasize early; they are occasionally of the spindle-cell type and have been known to metastasize by the blood stream to internal organs. All pigmented naevi of the hands and feet are subject to frequent trauma and therefore should be surgically excised while benign.

Congenital Origin.—There are at least five varieties of tumors of the hands and feet which are of congenital origin and can be satisfactorily explained by Cohnheim's theory of cell rests. One is the central

chondroma or enchondroma of the phalanges and metacarpal bones. Another is a rare cartilaginous tumor of the tendon sheath, occurring in multiple foci and often resembling abortive attempts to produce sesamoid bones (Fig. 2). A third is von Recklinghausen's type of generalized neurofibromatosis (Figs. 3 and 4). The hemangioma is a well-known congenital tumor (Figs. 5 and 6), as is the lipoma (Fig. 7).

Role of Trauma.—As previously stated, chronic irritation or repeated minor trauma has been accepted as a provocative cause of precancerous lesions and epitheliomas of the hands and feet. The evidence,

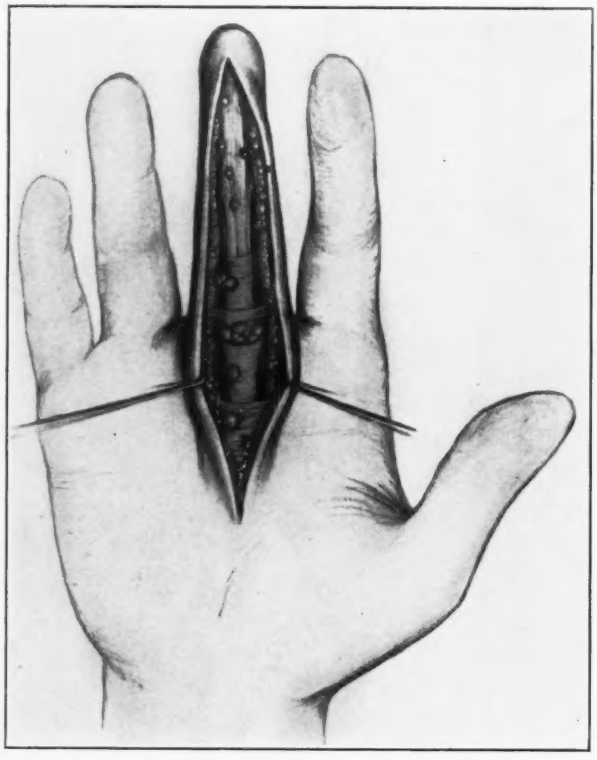


Fig. 2.—Multiple congenital benign chondromas of tendon sheath. They may have a histogenetic relationship to sesamoid bones.

especially in industrial workers, has been sufficiently conclusive to secure monetary compensation in court for such damages. A curious paradox exists in the case of the common corn or clavus, caused by chronic frictional irritation, a lesion that is markedly hyperkeratotic, yet having little or no tendency to become cancerous. A single or repeated injury to certain types of pigmented naevi may be responsible for their conversion into malignant melanomas, as testified by numerous clinical examples. Of greatest medicolegal importance, however, is the question whether or not a single trauma can induce a malignant tumor of the hands or feet. In seeking a solution to this problem, the

A. *B.*

Fig. 3.—*A*, Neurofibroma of toe; *B*, multiple congenital neurofibromas of hand in same patient as shown in *A*; note contractural deforminties so commonly occurring in this disease.

A. *B.* *C.*

Fig. 4.—*A*, Neurogenic sarcoma of low grade malignancy developing in hand, recurrent after excision. This patient had congenital neurofibromatosis of left hand and forearm. Note flexion and crossed deformities of fingers which was present at birth, a common neurogenic deformity. *B*, Dissected hand and wrist after amputation to show diffuse neurosarcoma of palm and wrist. *C*, Seven operations, including three amputations were done. Each time the diffuse neurosarcoma recurred higher up along the nerve trunks. An interscapulothoracic amputation was finally necessary. There has been no evidence of recurrence during the 3½ years intervening since this last operation.

Fig. 5.—Congenital diffuse hemangiomatosis of hand and foot in same patient. There is a coexistent hypertrophy of bones of the foot. Radiographic examination of the foot indicates that the hemangioma involves bone.

Fig. 6.—Congenital lymphangiomatosis of left foot and leg. Note the lymphangiectatic hyperkeratoses on medial aspect of left heel and between toes of left foot. The right leg is congenitally deformed, thus exaggerating the elephantiasis and overgrowth of long bones of the left lower leg. This phenomenon occurs occasionally with diffuse angiomatosis of an extremity. An ulcerating malignant endothelioma recently has developed on the medial aspect of the left ankle.

A. *B.*

Fig. 7.—*A*, Congenital lipomatosis of left hand and arm. Note relative sizes of right and left thumbs and deformity of left forefinger. *B*, After surgical excision of lipoma in left thenar region.

examiner should apply the postulates of Ewing concerning (1) the authenticity and adequacy of the trauma, (2) the previous integrity of the wounded part, (3) the origin of the tumor at the exact point of injury, (4) a reasonable time limit between the injury and the appearance of the tumor, and (5) the type of tumor resulting. The only malignant bone tumor of the hands and feet which is generally accepted to have a traumatic basis is the subperiosteal sarcoma; the mechanism here is probably disruption of the periosteum from the cortex with an intervening hematoma, organization of the blood clot, and later neoplastic hyperplasia. The same modus operandi probably occurs in the two other malignant tumors of possible traumatic origin; namely, malignant synovioma and liposarcoma. Almost every patient having a synovioma will relate a history of injury which seems to be authentic and adequate. Here again hemorrhage accompanies laceration of tendon sheaths and joint capsules and the normal reparative processes in some instances go on to the formation of a true synovial tumor, usually malignant. Some liposarcomas are unquestionably caused by a single acute injury. The adult type of liposarcoma with opaque granular cells is the one that follows trauma. Just as hemorrhage in muscle may lead to organization, calcification, osteogenesis, and occasionally the formation of an osteosarcoma, the same process in fat may result either in traumatic fat necrosis and healing with or without calcification or the stimulation of the adult fat cells to grow diffusely as a sarcoma possessing many grades of anaplasia and malignancy. As Ewing has said: "This type of liposarcoma represents the lawless phase of the growth of fat cells observed to a lesser degree in chronic inflammation of fat tissue." Dupuytren's contracture is really a diffuse neuromatous tumor occurring in the palm of the hand and developing after repeated chronic injuries, usually of the bruising type.

INCIDENCE OF TUMORS OF THE HANDS AND FEET

For the twenty-one-year period, Jan. 1, 1917, to Jan. 1, 1938, there were 573 tumors of the hands and feet treated at the Memorial Hospital for Cancer and Allied Diseases. The distribution of these 573 malignant and benign tumors according to site is shown in Table I. The upper extremities are more commonly involved, with 247, or 43.1

TABLE I

DISTRIBUTION OF MALIGNANT AND BENIGN TUMORS, ACCORDING TO SITE

SITE	TOTAL		MALIGNANT		BENIGN	
	NO.	%	NO.	%	NO.	%
Total	573	100.0	369	100.0	204	100.0
Hand	247	43.1	171	46.3	76	37.3
Finger	142	24.8	61	16.5	81	39.7
Foot	147	25.7	112	30.3	35	17.1
Toe	37	6.4	25	6.8	12	5.9

per cent, on the hand, and 142, or 24.8 per cent, on the fingers, together constituting more than two-thirds of all the tumors in this series. The largest proportion of the malignant tumors, 46.3 per cent, involves the hand, which might be expected from the fact that this site comprises the largest proportion of the total tumors.

Table II indicates the proportion of tumors at each site that are malignant and benign, with the foot showing the highest proportion among the malignant tumors of 76.2 per cent. In each regional location, with the exception of the fingers, the greater proportion of the tumors is malignant; phalangeal tumors, however, have a greater tendency to be benign, 57.0 per cent.

TABLE II

PROPORTION OF TUMORS AT EACH SITE WHICH ARE MALIGNANT AND BENIGN

SITE	TOTAL		MALIGNANT		BENIGN	
	NO.	%	NO.	%	NO.	%
Total	573	100.0	369	64.4	204	35.6
Hand	247	100.0	171	69.2	76	30.8
Finger	142	100.0	61	43.0	81	57.0
Foot	147	100.0	112	76.2	35	23.8
Toe	37	100.0	25	67.6	12	32.4

The various types of benign tumors of the hands and feet are shown in Table III. The largest proportion are papillomas (24.5 per cent) and angiomas (23.5 per cent). The giant cell tumor of tendon sheath (xanthoma) and pyogenic granuloma comprise 15.7 and 14.7 per cent, respectively, of the benign tumors.

TABLE III

DISTRIBUTION OF BENIGN TUMORS ACCORDING TO SITE AND TYPE OF TUMOR

TYPE OF TUMOR	TOTAL	HAND	FINGER	FOOT	TOE
Total	204	76	81	35	12
Chondroma	13	2	9	--	2
Giant cell tumor of tendon sheath (xanthoma)	32	12	17	3	--
Angioma, hemangioma, lymphangioma	48	19	16	12	1
Papilloma, cutaneous horn	50	24	17	8	1
Glomus tumor	5		5		
Lipoma	4	4			
Neuroma	22	10	2	8	2
Granuloma	30	5	15	4	6

The malignant tumors of the hands and feet are grouped in ten divisions, with the figures for the incidence of each type and site listed in Table IV. Epidermoid carcinoma comprised 180, or 48.8 per cent, of the 369 malignant tumors; two-thirds (124) of these cancers, or 68.9 per cent, were situated on the hands. The next largest group is the malignant melanoma, of which there were 105 tumors, or 28.5 per cent. In contrast to the epidermoid carcinoma, the largest proportion of melanomas were on the feet, 58 or 55.2 per cent.

TABLE IV

DISTRIBUTION OF MALIGNANT TUMORS ACCORDING TO SITE AND TYPE OF TUMOR

TYPE OF TUMOR	TOTAL	HAND	FINGER	FOOT	TOE
Total	369	171	61	112	25
Epidermoid carcinoma	180	124	32	20	4
Basal cell epithelioma, Sweat gland carcinoma, Adenoid cystic epithelioma	13	10	2	1	
Metastatic carcinoma	2	1	1		
Melanoma (malignant)	105	12	17	58	18
Osteogenic sarcoma, Periosteal sarcoma, Chondrosarcoma	8	2	1	3	2
Endothelial myeloma	1			1	
Malignant synovioma, Endothelioma of tendon sheath	19	7	4	8	
Neurogenic sarcoma	15	7	1	7	
Sarcoma of undetermined histogenesis: fibrosarcoma myxosarcoma	16	7	3	6	
Kaposi's sarcoma	10	1		8	1

CURABILITY OF TUMORS OF THE HANDS AND FEET

Many difficulties attend any attempt to analyze the end results of treatment of malignant tumors of the hand and feet. Each histologic type should be considered as an entity. The results vary also with the degree of anaplasia, the local extent or depth of infiltration, the presence of metastases in regional lymph nodes, the tendency to visceral involvement, the coexistence or later development of multiple tumors

TABLE V

PROPORTION OF MALIGNANT TUMORS OCCURRING ON THE HAND AND FOOT

TYPE OF TUMOR	TOTAL CASES ENTIRE BODY	HAND AND FOOT NO.	HAND AND FOOT %
Epidermoid carcinoma of skin (exclusive of genitals and lip)	1,584	180	11.6
Basal cell epithelioma	2,189	13	0.6
Malignant melanoma	481	105	21.8
Osteogenic sarcoma	644	8	1.2
Malignant synovioma, Endothelioma of tendon sheath	99	19	19.3
Neurogenic sarcoma	484	15	3.9
Sarcoma unclassified	204	16	7.8

of the same type in the same patient, the inherent incurability of a disease that is of generalized distribution, and the age of the patient. An epithelioma that has invaded the deep fascia and become fixed will require more radical treatment than one which is confined to skin and is readily movable. The metastatic involvement of regional lymph nodes by malignant melanoma and epidermoid carcinoma unfavorably influences the prognosis; radical axillary or groin dissection is necessary to supplement the treatment of the primary lesion. Pulmonary metastasis may occur so early in the history of osteosarcoma and ma-

lignant synovioma as to nullify the good effect of local treatment, however radical. In the case of Kaposi's idiopathic sarcoma, any single nodule can be destroyed, but the slow progressive generalization of the disease is so inevitable that control rather than cure is the object of treatment.

The regional location of these malignant tumors is peculiarly favorable for curative treatment either by surgical or radiologic means, as indicated. Conservative surgical measures sparing a functional part of the foot or hand sometimes are possible.

The end results of treatment of epidermoid carcinomas of the hands and feet are really better than the figures herein submitted. Epitheliomas of the extremities occur at an average age almost ten years older than in epitheliomas of the face and lip. These elderly patients, many of whom are more than 70 years old, are difficult to keep under observation; they may die of intercurrent diseases while under treatment or before the five-year period which is generally accepted as the criterion for cure has passed. For example, in Table VI, dealing with the end results of epidermoid carcinomas of the hands and feet, 82 patients were lost to observation and analysis. Of this group, 53 patients either received no treatment, refused treatment, were treated elsewhere, or did not complete the treatment outlined at the Memorial Hospital. Of the remaining 39 patients who were treated but subsequently could not be found, 19 were clinically free of cancer more than two years after treatment and 11 were known to have no evidence three or more years after treatment had been instituted.

TABLE VI

EPIDERMOID CARCINOMAS OF HANDS AND FEET

END RESULTS OF TREATMENT

END RESULTS		NUMBER		PER CENT
Total patients		180		
Lost to observation		82		
Number available for study of end results		98		100.0
Dead		36		36.7
Living with evidence (total)		13		13.2
Less than 5 yr.	9		9.2	
5 or more yr.	4		4.1	
Living with no evidence (total)		49		50.0
Less than 5 yr.	19		19.3	
5 to 10 yr.	26		26.4	
10 or more yr.	4		4.1	

End Results of Epitheliomas of Hands and Feet Metastatic to Regional Lymph Nodes.—Theoretically all epitheliomas of the hands and feet should be cured before metastasis occurs, if our statistics are correct, as they reveal the fact that the average interval between the first appearance of the carcinoma and the recognition of nodal metastasis is three years. The decision to be made concerning prophylactic

TABLE VII

EPIDERMOID CARCINOMAS OF HANDS AND FEET

END RESULTS IN RELATION TO SITE OF TUMOR

END RESULTS	HAND		FINGER		FOOT		TOE	
	NO.	%	NO.	%	NO.	%	NO.	%
Total patients	124		32		20		4	
Lost to observation	60		15		7			
No. available for study of end results	64	100.0	17	100.0	13	100.0	4	100.0
Dead	24	37.5	7	41.2	3	23.0	2	50.0
Living with evidence	4	6.3	3	17.6	6	46.2		
Living with no evidence	36	56.2	7	41.2	4	30.8	2	50.0

dissection of regional lymph nodes when there is no clinical evidence of their involvement must be influenced by the fact that 24 per cent

TABLE VIII

END RESULTS OF TREATMENT FOR MISCELLANEOUS TUMORS OF HANDS AND FEET

END RESULTS	TYPES OF TUMOR							
	SARCOMA UNCLASSIFIED		SYNOVIOMA		NEUROSARCOMA			
Total patients		16		19		15		
Lost to observation		7		5		7		
No. available for study of end results		9		14		8		
Dead (total)		5		4		1		
Living with evidence (total)		1		7		1		
Within 1 yr. of admission	1		3					
1 to 5 yr.			3		1			
5 or more yr.			1					
Living with no evidence (total)		3		3		6		
Within 1 yr. of admission	1				1			
1 to 5 yr.	1		2		5			
5 or more yr.	1		1					

of our patients admitted with epidermoid carcinomas of the hands and feet and without palpable lymph nodes in axilla and groin subsequently developed nodal metastases while under observation. In a

TABLE IX

MALIGNANT MELANOMA OF HANDS AND FEET

END RESULTS OF TREATMENT

END RESULTS	NUMBER		PER CENT
Total patients	105		
Lost to observation	16		
No. available for study of end results	89		100.0
Dead (total)	58		65.1
Living with evidence (total)	11		12.4
Within 1 yr. of admission	5	5.6	
Over 1 yr.	6	6.7	
Living with no evidence (total)	20		22.4
1 to 3 yr.	4	4.5	
3 to 5 yr.	7	7.9	
5 to 10 yr.	7	7.9	
10 or more yr.	2	2.2	

series of 17 axillary dissections for metastatic carcinoma of the hand, 6 (35 per cent) of these patients subsequently died and 11 are now living and well; 5 of this group were operated upon more than five years ago. Of 7 inguinal dissections for metastatic carcinoma of the foot, 2 of these patients are dead and 5 are living and well; 3 of this group were operated upon more than five years ago.

TABLE X

MALIGNANT MELANOMA OF HANDS AND FEET

END RESULTS IN RELATION TO SITE OF TUMOR

END RESULTS	HAND		FINGER		FOOT		TOE	
	NO.	%	NO.	%	NO.	%	NO.	%
Total patients	12		17		58		18	
Lost to observation	3		3		10			
No. available for study of end results	9	100.0	14	100.0	48	100.0	18	100.0
Dead (total)	3	33.3	5	35.7	37	77.0	13	72.2
Living with evidence	3	33.3	3	21.4	3	6.3	2	11.1
Living with no evidence	3	33.3	6	42.9	8	16.7*	3	16.7

*In contradistinction to the epidermoid carcinomas, the incidence of melanomas is greater on the foot than on the hand. The curability of melanomas of the foot is only one-half as great as the curability of melanomas of the hand. It has long been known that the prognosis of melanoma of the foot is worse than for melanoma of the hand.

End Results of Melanomas of Hands and Feet Metastatic to Regional Lymph Nodes.—In a series of 32 axillary dissections for metastatic melanoma of the upper extremities (including arm and forearm as well as hand), 19 of these patients subsequently died and 13 are living and well; 4 of this group were operated upon more than five years ago. In a similar series of 31 inguinal dissections for metastatic melanoma of the lower extremities, 24 of these patients are now dead and only 7 are living and well; 5 of this group have fulfilled the criterion of five-year cure. Twenty-six patients received radiation therapy as the sole method of treatment of metastatic melanoma in inguinal and axillary lymph nodes. Such treatments consisted of combinations of external irradiation with high voltage x-rays or radium element pack and interstitial radium therapy. Only 2 of these 26 patients are now living and without clinical evidence of metastatic melanoma; the periods of observation, however, are less than three years.

The distinction between radiosensitive and radioresistant tumors of the hands and feet is not absolute. In this connection it should be noted that radiosensitivity and radiocurability are not synonymous terms. A radiosensitive tumor, such as lymphosarcoma, may respond phenomenally well to irradiation, yet destroy the patient because of early and widespread metastases. On the other hand, certain slow-growing and radioresistant fibrosarcomas may slowly but completely regress after long-continued irradiation.

RADIATION THERAPY OF TUMORS OF HANDS AND FEET

CLASSIFICATION OF RADIOSENSITIVITY

TABLE XI

CLASSIFICATION OF RADIOSENSITIVITY

RADIOSENSITIVE	RADIORESISTANT
Benign Tumors	
Wart	Fibroepithelial tumor
Epithelial papilloma	Neuronaevus
Hemangioma	Lipoma
Granuloma	Neurofibroma
	Lymphangioma
	Glomus tumor
	Giant cell tumor of tendon sheath (xanthoma)
	Chondroma
	Osteoma
Malignant Tumors	
Epidermoid carcinoma	Osteosarcoma
Basal cell carcinoma	Melanoma
Kaposi's sarcoma	Spindle cell sarcoma
Endothelial myeloma	Myxosarcoma
	Neurosarcoma
	Synovioma

None of the nine common benign tumors in the radioresistant group should ever be treated by any form of radiation therapy. Epithelial warts and papillomas readily regress after small doses of unfiltered low voltage x-radiation, or by the application of the beta ray of radium applied through the medium of a radon bulb (Fig. 12). The hemangiomas vary greatly in radiosensitivity; the cavernous hemangiomas regress by thrombosis, organization, and obliteration (Fig. 8) following the surface application of radium or low voltage x-rays. In the more radioresistant hemangiomas, small doses of interstitial radium therapy, either by gold radon seeds or radium element needles, may be necessary to complete the disappearance of tumor. Hemangiomas, as a rule, are much more radiosensitive in infancy than they are in childhood and later life; with added years, the endothelial cells and blood vessels comprising the tumor lose their embryonal and therefore radiosensitive character. Pyogenic granulomas, occurring quite frequently in the nail sulci, are not readily amenable to surgical treatment because of the frequency of recurrence; small doses of lightly filtered radiation, either by low voltage x-rays or radium, will suffice to cause complete disappearance of this tumor with practically no discernible scar.

In the group of malignant tumors of the hands and feet, radiation therapy should never supplant surgical excision or amputation as the sole method of treatment of osteosarcoma, malignant melanoma, spindle cell sarcoma, and myxosarcomas of undetermined histogenesis. If the

sarcomas are inoperable, radiation therapy may afford some palliation by the exercise of growth restraint. Radical surgical treatment is the method of choice for most neurosarcomas and malignant synoviomas, but irradiation is often a useful adjunct to surgical treatment, being used either preoperatively or postoperatively, or both. Some cures have been effected by radiation therapy alone, but the prospect of cure is not great. After careful fractionated irradiation by high voltage roentgen rays, the neurosarcomas and malignant synoviomas may slowly diminish in size; this regression is never dramatic in its rapidity, but it is a progressive, gradual replacement of the tumor by dense, fibrous tissue producing a condition termed by Ewing "abortive fibrosis" (Fig. 9). Although the operative wounds made following such radiation therapy are of slow healing, the end result may justify such preoperative irradiation, as local recurrence is seldom the rule.

A. *B.*

Fig. 8.—*A*, Congenital hemangioma of dorsum of foot; *B*, result of radiation therapy.

The superficial epidermoid carcinomas and the less frequent basal cell epitheliomas of the hands and feet readily can be cured by the application of radium plaques (Fig. 11) or by contact or short distance low voltage roentgen therapy (Fig. 10) or by the usual method of low voltage roentgen therapy. Although radiation cures of these tumors are possible of accomplishment, this method is not always indicated, as there is great danger of late radiation necrosis, particularly if the cancers are situated on the dorsum of the hand or foot in close proximity to bone, where there is not an abundance of underlying soft tissues. It is for this reason that many of the epitheliomas of hands and feet are better treated by surgical excision and skin grafting. With improvement in the technique of radiation therapy, particularly the new modalities that have recently come into use, and with full appreciation of the hazards encountered, the radiologist may secure

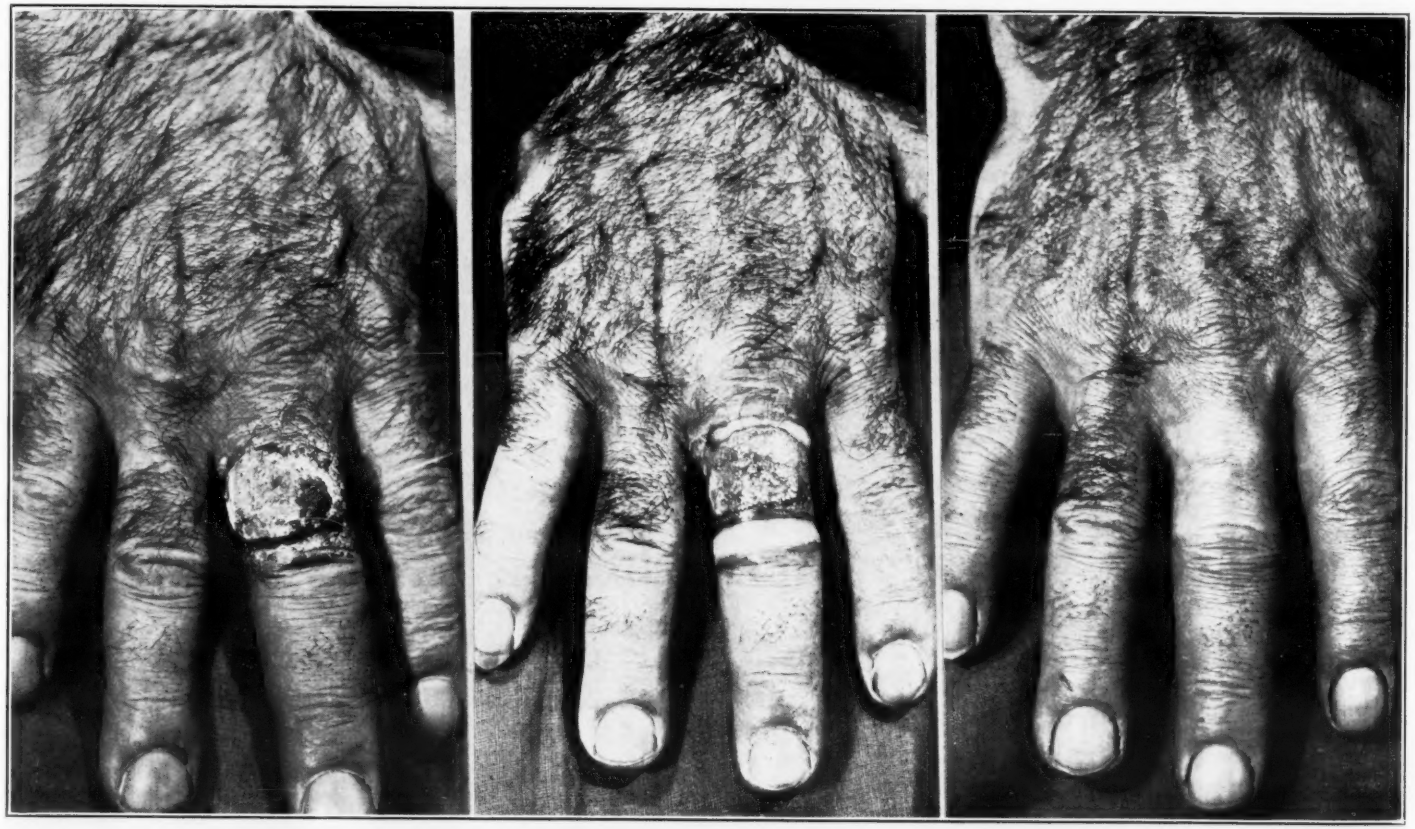
good results, providing the epithelioma does not infiltrate into tendon or bone.

The endothelial myeloma, or Ewing's tumor of bone, as a rule is quite radiosensitive, diminishing early and rapidly after exposure to roentgen rays. The immediate and seemingly complete clinical disappearance of this tumor may give one a false impression of security, because it is usually found that even intensive irradiation does not completely sterilize the endothelial myeloma. On this account, it is deemed imperative in most instances to follow such irradiation by amputation in those cases where the tumor has a single focus in bone. Wherever there are multiple endothelial myelomas, then, of course,

Fig. 9.—*A*, Recurrent adherent malignant synovioma, occurring in a young pregnant woman. *B*, Complete clinical regression following high voltage roentgen therapy. The factors were: 200 kv., 35 cm. target-skin distance, 0.5 mm. Cu + mm. Al filter, circular cone delimiting field as shown, anterior and posterior cross-firing fields, 300 r. units daily, alternating until each field received 3,600 r. units.

the possible curative value of amputation must be denied the patient in favor of the known palliative effect of roentgen therapy.

Insomuch as the idiopathic hemorrhagic sarcoma of Kaposi is of multicentric origin, attempts at surgical control usually are futile. As many as five to ten, or even twenty, of these independent primary tumors may develop at the same time on both lower extremities. These nodules are not secondary extensions of a single primary sarcoma, but represent new independent foci of the disease which have a common underlying basis. It is well known that these sarcomas develop usually on the lower extremities of middle-aged men, the majority of whom have some circulatory disturbances. In one sense it is a generalized



A. *B.* *C.*

Fig. 10.—*A*, Epidermoid carcinoma of skin of finger. An occupational cancer occurring in a mechanic whose hands were constantly immersed in tar and oil (July 31, 1936). *B*, Height of radiation reaction (Sept. 11, 1936). After low-voltage x-ray therapy, using the following factors: 100 kv., 30 cm. target-skin distance, 3 mm. Al filter, size of field as shown in illustration, 250 r. units daily to single port for total dose of 4,000 r. units. *C*, Result after healing (Dec. 4, 1936).

or systemic disease, although it may require years for the remainder of the body to be involved. This being the case, radiation therapy is definitely indicated as the sole method of treatment. Kaposi's sarcomas vary greatly in their histologic make-up, due to the fact that they originate from such a complex structure; namely, the neurovas-

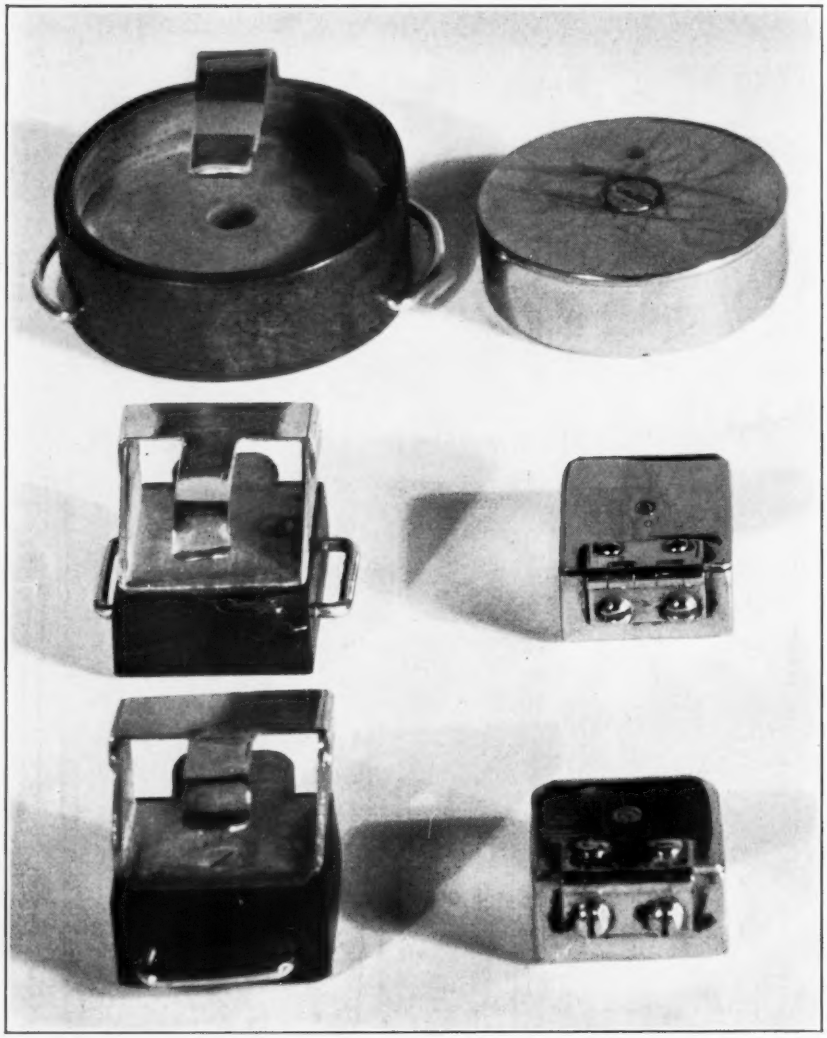


Fig. 11.—Radium plaques of various dimensions used as standard applicators for hemangiomas, epitheliomas, Kaposi's tumors, and other superficial neoplasms of the hands and feet. The bakelite blocks with safety catches are first applied over the tumor and furnish a radium skin distance of 1 cm., after which the radium plaques are slipped onto the blocks with a minimum of handling.

cular annexes in the skin and subcutaneous tissues. Hence, some of them are more angiomatous, others are neurosarcomatous, etc. Low voltage roentgen therapy, the topical application of radium by means of plaques applied at short distances, and contact radiation with low voltage x-rays or a radon bulb afford satisfactory methods of control.

EQUIPMENT FOR RADIATION THERAPY OF TUMORS OF THE HANDS AND FEET

Radium Therapy.—The superficial tumors of the skin, e.g., epitheliomas, Kaposi's sarcoma, hemangioma, may be treated by standardized radium applicators of variable sizes. There are four standard radium applicators in general use at the Memorial Hospital and their different surface areas render them suitable for treating many small tumors of the skin and subcutaneous tissues (Fig. 11). The filtration of these plaques is the equivalent of 3 mm. brass. They are applied at a radium skin distance of 1 cm. with the exception of the tray which has a radium skin distance of 3 cm. Small blocks of balsa wood or bakelite are used to maintain this distance. The region surrounding the cancer is shielded by heavy lead to protect the normal adjacent tissues.

TABLE XII

TYPE	SIZE	AREA RADIATING SURFACE	FILTER	DISTANCE	DOSE MG. HR.
Square plaque	1.8 cm. square	2 sq. cm.	2 mm. brass + 0.2 mm. Pt.	1 cm.	700-1,000
Long plaque	2.7 × 1.7 cm.	3.75 sq. cm.	2 mm. brass + 0.2 mm. Pt.	1 cm.	900-1,200
Round plaque	4 cm. diameter	7 sq. cm.	2 mm. brass + 0.2 mm. Pt.	1 cm.	1,200-1,600
Tray	6.2 cm. diameter	17.5 sq. cm.	2 mm. brass + 0.2 mm. Pt.	3 cm.	3,000-4,000

Gold Radon Seeds.—These radon seeds for interstitial irradiation are 4 mm. long. They contain variable quantities of radon, usually 1.2 to 3 mc. per seed. The seeds are inserted into tumors using sterile precautions and they remain permanently in the tumor long after the radon has been completely dissipated. The dose necessary for tumors of various diameters, depending on the number of threshold erythema units required, is given in Table XIII. The figures in the table are true only when the radon is implanted in the central half of the tumor mass; if radon seeds are placed throughout the tumor at intervals of 1 cm., the quantity of radon employed should be increased by 25 per cent in order to arrive at the same dose in threshold erythema units. Gold radon seeds are indicated whenever interstitial radon is desired as an adjunct to contact or short distance radium or roentgen therapy. Care must be taken that the seeds are not inserted too near cartilage or bone, else a painful and chronic perichondritis or periostitis may follow.

TABLE XIII

QUANTITIES OF RADIATION NECESSARY TO DELIVER SPECIFIED MINIMUM DOSES IN VARIOUS VOLUMES* INTERSTITIAL SOURCES, FILTER 0.3-0.5 MM. GOLD

THRESHOLD DOSES	VOLUME (C.C.)						
	10	20	30	40	60	80	100
	Mc. or Mg. Hr.						
1	275	380	470	530	650	750	845
2	550	760	940	1060	1300	1500	1690
3	825	1140	1410	1590	1950	2250	2535
4	1100	1520	1880	2120	2600	3000	3380
5	1375	1900	2350	2650	3250	3750	4225
7	1925	2660	3290	3710	4550	5250	5915
10	2750	3800	4700	5300	6500	7500	8450

*These doses are for needles to be left in place four days or longer. If they are to be removed in a shorter time, all quantities of radiation should be somewhat smaller (Quimby; Am. J. Roentgenol.).

Radon Bulb.—Radon in the quantity of 300 to 600 mc. is collected at intervals and pumped into a small glass sphere, which is imbedded in a wax cup at the end of a long handle (Fig. 12). This glass radon sphere or bulb is placed in direct contact with lesions of the skin to give doses, varying from 150 to 500 mc. minutes. As glass is the only filter, the radiation emitted is about 97 per cent beta rays and 3 per cent gamma rays. The use of this applicator therefore is limited to precancerous lesions of the skin, particularly keratoses.

High voltage roentgen rays with peak kilovoltage of 200 or more are seldom used in the treatment of skin cancers, except for deeply infiltrating epitheliomas. The more deeply situated synoviomas, neurosarcomas, fibrosarcomas, and bone tumors are treated by this modality for the indications previously mentioned. Limitation or restriction of the field of irradiation, cross-firing through dorsal and palmar or solar surfaces, and administration of daily small fractionated doses are the principles of treatment now almost universally adopted.

Low voltage roentgen rays of 100 to 140 peak kilovolts are important in the treatment of superficial benign and malignant tumors of the extremities, particularly epitheliomas. A target skin distance of 20 to 30 cm. is used, either without a filter or with 1 to 3 mm. of aluminium added, depending on the depth dose desired. Higher voltages, greater target skin distance, and heavier filters are indicated whenever an increased depth dose is needed for thick or deeply infiltrating cancers. Lower voltage, shorter target skin distance, and less filter or no filter at all are indicated for the superficial tumors. The normal skin surrounding the tumor to be treated is shielded with lead during an x-ray treatment. If x-rays of low intensity (100 kv.) are used, 1 mm. of lead will remove 99 plus per cent of the radiation, thus allowing ample protection. This thin sheet lead is easily cut and moulded to fit each individual epithelioma or hemangioma. The lead protective shields, when made, are then held in place with adhesive

plaster or by contact pressure from the various sized cylinders which are attached to the open port for the purpose of limiting the field of irradiation. Correction in the roentgen dose at the surface must be made when these shields and cones are used, because only the central portion of the beam is utilized. It is a well known physical law that the smaller the field, the less the depth dose obtained, due largely to a decrease in the scattered tissue radiation. Daily fractionated doses of 150, 200, or 250 roentgens are given until the total dose approximates 2,500 to 4,000 roentgens for malignant tumors. For heman-

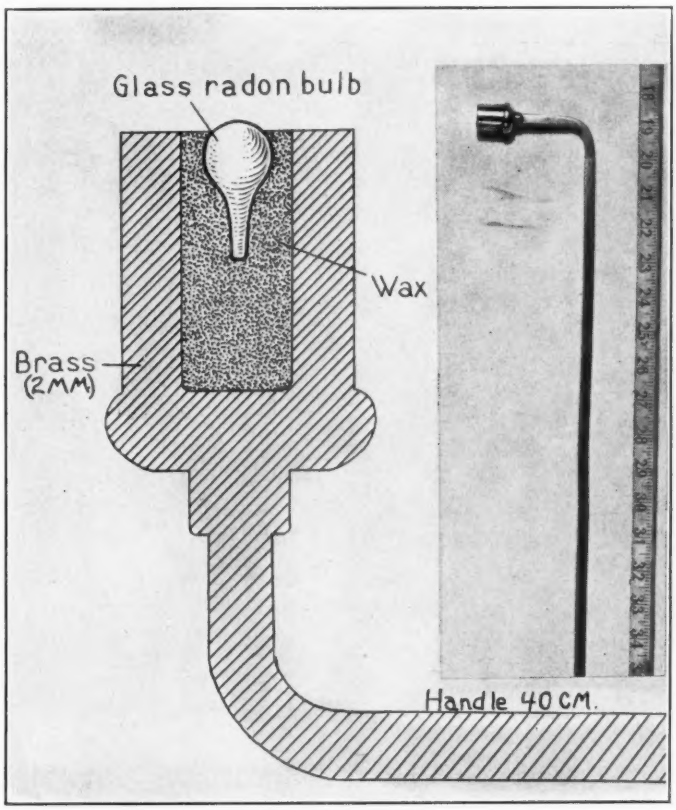


Fig. 12.—Radon bulb. This is made up once in three weeks at the Memorial Hospital. Since glass is used as a filter, the emanation is about 97 per cent beta and 3 per cent gamma. Its use is therefore restricted to very small and superficial basal cell carcinomas less than 1 mm. in thickness and precancerous lesions. Dosage is in "millicurie minutes," and varies between 200 and 600.

giomas doses of 150 to 300 roentgens may be given at weekly intervals for total doses seldom amounting to more than 1,500 r. units.

Chaoul Contact or Short Distance Roentgen Therapy.—During the past decade, physicists and radiologists have devoted considerable attention to the construction of low voltage x-ray machines which combine the advantages of radium dose distribution (as used for surface application) and the economy, efficacy, and convenience of the x-rays. Special x-ray tubes furnishing a dose distribution similar to contact

or superficial radium therapy were designed many years ago and then abandoned because of technical difficulties concerned with the prevention of shock to the patient. These difficulties were subsequently overcome and the short-distance or contact x-ray method was developed. Schaefer and Witte, of Göttingen, Germany, experimented in 1929 using a Lenard tube and cathode rays only; they later added a metal filter over the tube which did not permit the emergence of the cathode beam and served as the anode or target. The thin copper filter or transmission anode was plane, planoconcave, or planoconvex to modify the shape and focal sharpness of the emergent beam. Chaoul, of the

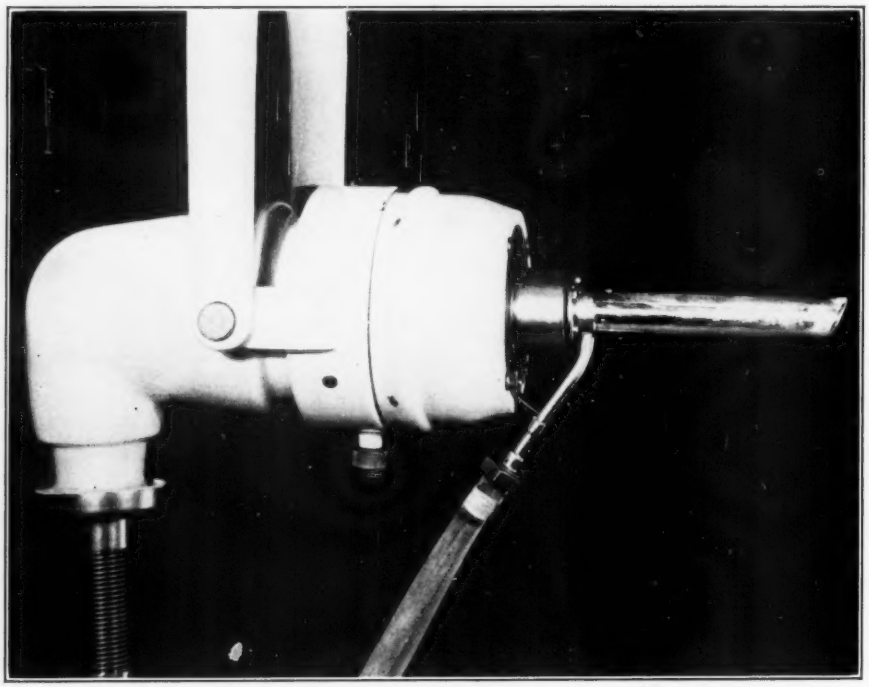


Fig. 13.—Chaoul low voltage contact x-ray tube with tube holder. The target is in the extreme tip of the narrow cylinder. The attached rubber tubes at the base of the cylinder are for the water-cooling system. The unit is about the size of the average dental radiographic outfit, yet is capable of intensive and effective low voltage x-ray therapy.

Charité Surgical Clinic, Berlin, designed a similar apparatus for low voltage, short-distance, or contact x-ray therapy, which was limited to a voltage range of 50 to 60 kv. with a filtration of 0.2 mm. of copper. The anode is so placed that the tube operates at contact or 3 to 5 cm. target skin distance. (Fig. 13.) It has applicators or cones of various sizes and shapes to place against the cancers to be treated. The Chaoul machine is water cooled and shockproof.

The short-distance or contact x-ray treatments make possible the delivery of doses to the tumor sufficient to disintegrate tumor cells and yet spare the healthy surrounding tumor bed by using small fields

sharply localized about the tumor. It furnishes limitation of depth effect by producing a steep energy gradient. The latter is obtained by decreasing the target skin distance and the voltage delivered to the tube. With this apparatus, a soft x-ray beam is utilized and these rays are absorbed in the superficial tissues. For contact application, the dosage rate is approximately 800 r. units per minute; for a target skin distance of 3 cm., it is approximately 88 r. units per minute; and for a target skin distance of 5 cm., it is approximately 36 r. units per minute. This apparatus, of course, has only a specialized usefulness for the treatment of superficial tumors of the hands and feet. Because the depth dose is not great, and the major portion of the radiant energy is absorbed by the tumor proper, the deeper structures

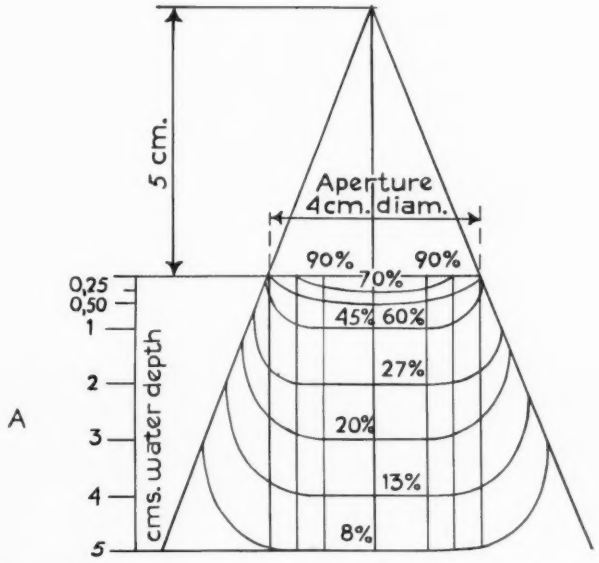


Fig. 14.—Isodose chart with 5 cm. F.S.D., 60 kv.; filter 0.2 mm. Cu; aperture of applicator, 4 cm. diameter.

of the hands and feet are uninjured and the hazards of late radiation necrosis are considerably lessened. The reaction is sharply circumscribed around the cancer. For epitheliomas of the hands and feet, we have used daily fractions of 250 to 400 r. units with total dosages ranging anywhere from 3,000 to 8,000 r. units, depending on the dimensions and radiosensitivity of the cancer. (Fig. 14.)

Philips Contact Roentgen Therapy.—A more flexible and equally serviceable unit has been designed by Philips (Fig. 15). This complete outfit is contained in a small portable cabinet, mounted on casters and weighing 325 pounds. It can be used in any room that contains an outlet for 110 volt alternating current. The high tension transformers, the filament transformers for the tube and the valve, the condenser, the blower which supplies the air for the cooling of the tube, and all

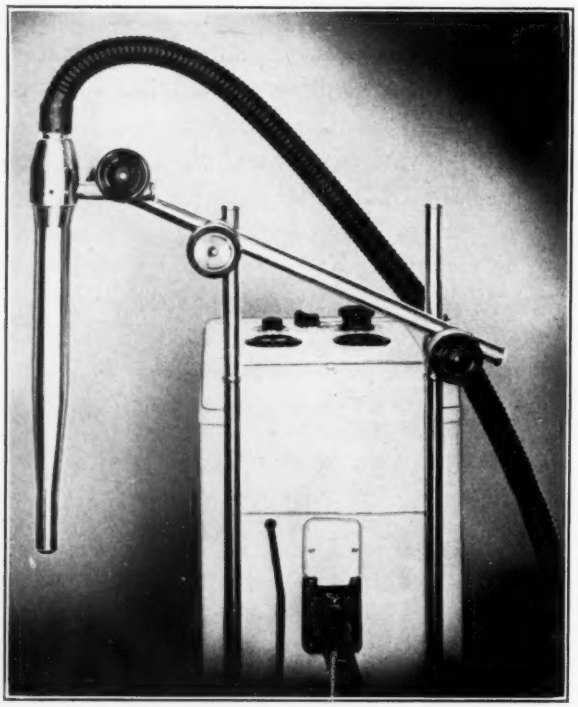


Fig. 15.—Philips low voltage contact x-ray outfit. The aircooled x-ray tube is within the long proboscis-like cylinder. The target is at the extreme end of this tube. The handle may be disengaged from the standard and held with the hands while treatment is in progress. The rubber-covered cable, 2 M. in length, permits great flexibility.

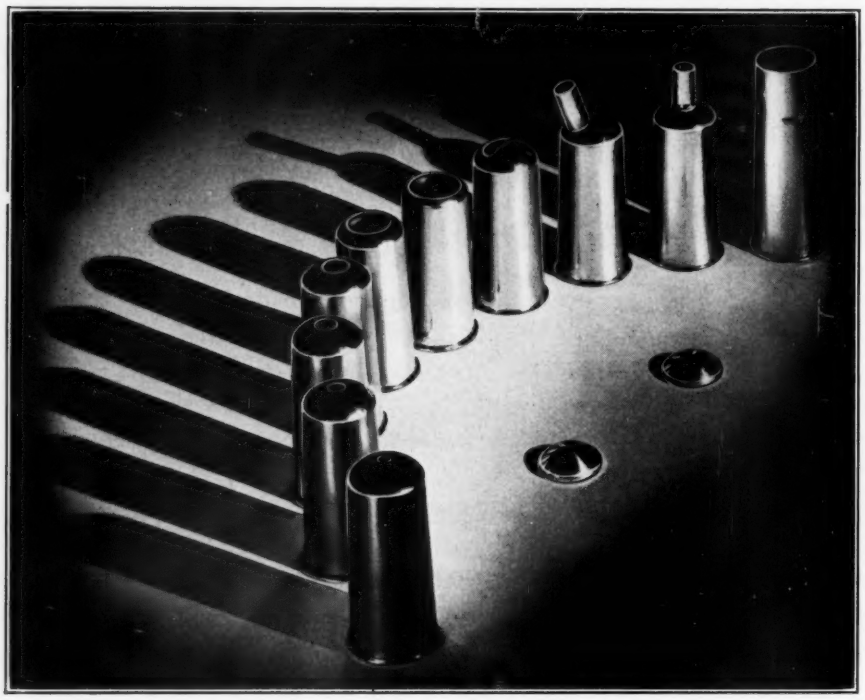


Fig. 16.—Cones and additional aluminium filters for the Philips contact x-ray tube. These cones provide outlets of different shapes and dimensions for superficial tumors and precancerous lesions.

other component parts except the tube itself are contained within the compact cabinet. A shockproof flexible cable, 2 M. in length, connects the tube to the unit. The x-ray tube is shockproof and is unipolar, the cathode side being grounded. As in the Chaoul machine, the x-rays emerge axially. The cooling air passes through the hose arranged around the shockproof cable and leaves the tube by orifices provided on the tube.

The inherent filter of the tube and shockproof shield is the equivalent of only 0.2 mm. Al. If additional filtration is deemed necessary, disks of 1 or 2.5 mm. Al thickness may be inserted over the tube end and held in place by attached treatment cones (Fig. 16).

The diameter of the emergent x-ray beam is slightly less than 2 inches, therefore the fields to be irradiated must be necessarily small. If tumors of greater surface area are to be treated, as frequently occurs for epitheliomas and hemangiomas, the lesions are subdivided into multiple fields or ports.

The distance of the focus from the target to the protection cap over the tube end is 18 mm. Over this tube end is placed a localizing cone which increases the inherent target contact distance to 2 cm. The intensity is always at 50 kv. constant potential. Two milliamperes is the current employed, although the tube is capable of functioning with 3 Ma. if the time of treatment is short.

TABLE XIV

PHILIPS CONTACT X-RAY TUBE (50 KV.—2 MA.)

DOSE IN R.	TIME IN SECONDS (″) OR MINUTES (′)		
	0.0 MM. AL	1.0 MM. AL	2.5 MM. AL
T.S.D.			
Contact (20 Mm.)			
500	3½″	13″	38″
1,000	7″	27″	1′ 16″
1,500	10″	41″	1′ 54″
2,000	14″	55″	2′ 32″
2,500	17″	1′ 8″	3′ 10″
3,000	21″	1′ 22″	3′ 48″
r./min.	8,700	2,200	790

DOSE IN R.	TIME IN MINUTES (′) OR SECONDS (″)		
	0.0 MM. AL	1.0 MM. AL	2.5 MM. AL
	T.S.D.		
2 Cm. From Surface (40 Mm.)			
500	13″	1′ 8″	2′ 42″
1,000	27″	2′ 16″	5′ 25″
1,500	40″	3′ 25″	8′ 7″
2,000	53″	4′ 33″	10′ 48″
2,500	1′ 6″	5′ 41″	13′ 31″
3,000	1′ 20″	6′ 49″	17′ 14″
r./min.	2,250	440	185

The actual tube is within a long, light, metal cylinder which is handled at will by means of an attached grip. It may be held by the hands during treatment, or, if a long treatment is planned, the tube may be supported by standards attached to the unit.

The indications are the same as those mentioned for the Chaoul machine. There is a distinct advantage, however, in the roentgen output of the Philips tube, which is so great that only a very short time is necessary to complete any treatment. The total dose administered for skin tumors of the hands and feet varies from 1,500 r. units for hemangiomas to 8,000 r. units (2 cm. distance) for epitheliomas.

CARCINOMA OF THE HANDS AND FEET

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ALTHOUGH carcinoma vies with fibrosarcoma in being the most frequently occurring malignant tumor of the soft tissues of the extremities, its incidence is not great and only some 5 to 10 per cent of cutaneous carcinomas occur on the hand and foot (Desaive, De Asis, DeBell, Stevenson, Geschickter, Koehler, Knowles, and Sigel).

The upper extremity is affected two to three times as frequently as the lower, an incidence which argues for the importance of trauma as a factor, although the nature of the irritative agent is not always clear. The chronic irritation which leads to calluses on the hands and corns on the feet never produces carcinoma nor is carcinoma prone to occur on the basis of a varicose ulcer; in fact, its occurrence there is of the greatest rarity.

Carcinomas of the extremities may be classified into three large groups, according to apparent etiologic factors. This subdivision must be arbitrary since the actual significance of any of the assumed etiologic factors is unknown. A convenient grouping is as follows:*

I. Carcinomas arising in connection with trauma or irritation
   a. Irradiation
      X-ray
      Radium
      Solar (such as exemplified by senile keratoses, keratoses in sailors, farmers, etc.)
   b. Chemical irritation, external (e.g., tar, anilin, pitch, etc.)
      Internal (arsenic)
   c. Chronic mechanical irritation
   d. Scar tissue irritation (burn scar especially)
   e. Irritation from a single trauma or chronic infection, syphilitic ulcer, varicose ulcer, etc.

II. Carcinoma arising in some previous skin tumor

III. Carcinoma arising from normal skin

X-Ray and Radium Dermatitis and Carcinoma.—Ouidin in 1897 recognized that dermatitis and epithelioma may follow exposure to roentgen irradiation, but his early warning was not seriously taken, and as a result the medical profession has furnished and still is furnishing

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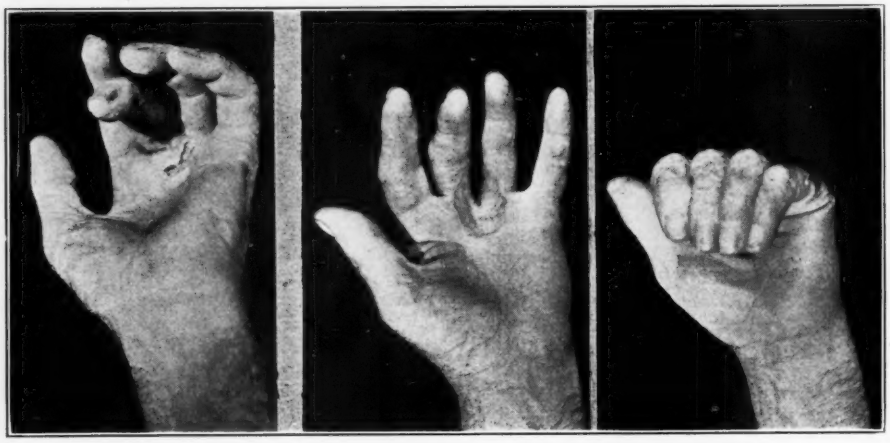
*Adair, in describing briefly the various types of epitheliomas of the hand, has classified them into six groups, those occurring: (1) in the aged, (2) as result of exposure to the elements, (3) in burn scars, (4) subsequent to internal medication, (5) following chemical irritation, and (6) following x-rays and radium irradiation.

many martyrs to the x-ray. The professional radiologist has learned to protect himself from the cumulative effects of adventitious irradiation incident to manipulation and fluoroscopy. The general practitioner, however, who uses the x-ray incidental to his practice is exposed to minute doses of irradiation over a long period of time. The great majority of patients presenting themselves for treatment of irradiation dermatitis and carcinoma are practicing physicians and surgeons and not professional roentgenologists. (Figs. 1-3.)

The chronic irradiation dermatitis which subsequently exhibits carcinomatous changes must be distinguished from the acute dermatitis which follows excessive exposure over a short period of time. The acute dermatitis may produce painful ulceration and weeks or months may be required to bring about healing; rarely however does carcinoma develop in it.



A. *B.*

Fig. 1.—*A*, Precancerous hyperplasia of hand due to irradiation (P.M.H. 8114, 1931). Thirty years previous to admission to hospital the patient, a 69-year-old doctor, began to use the x-rays in examination of patients. Shortly afterwards a dermatitis developed and later a few areas of keratosis which were removed with radium. The skin remained rough and inflamed, but no serious trouble developed until 1929 (almost twenty-eight years after the onset) when a fissure, the size of a navy bean, appeared between the ring and middle fingers. The fissure persisted without symptoms for a year, at which time radium was applied and the fissure disappeared for a month. A recurrence of the ulcer was treated again with radium and this time the ulceration became larger and very painful and a second ulcer developed in the palm. These ulcers were excised and the raw area covered with a split graft in October, 1931. Healing occurred and there was no recurrence of the condiiton at the time of death from some other cause some twenty months later. *B*, Condition of hand five months after application of split graft. *C*, Photomicrographs of the tissues removed from the patient shown in *A*, showing the endarteritis and fibrosis of the subcutaneous tissues and the inflammatory hyperplasia (precancerous) of the skin at the margin of the ulcer,

The manner in which irradiation leads to the peculiar changes in the skin and subcutaneous tissues which lead up to keratosis, ulceration, and finally carcinoma is a matter of controversy. It is not known whether there is a direct action of the rays upon the skin or whether irradiation produces its effects through the intermedium of some chemical substance released by the rays. Porter and Wolbach believed that the rays had an especial affinity for collagen and that this sub-

stance, particularly in the walls of the blood vessels, became thick and swollen and was later replaced by fibrous tissue (Fig. 1*C*). Flaskamp, along with Rost, believes that the rays attack the cells directly and that the effect which is most felt in the nucleus is noted also in the cytoplasm. Because of the spottiness of the injury, repair may occur, provided of course repeated damage is not done; but with continued

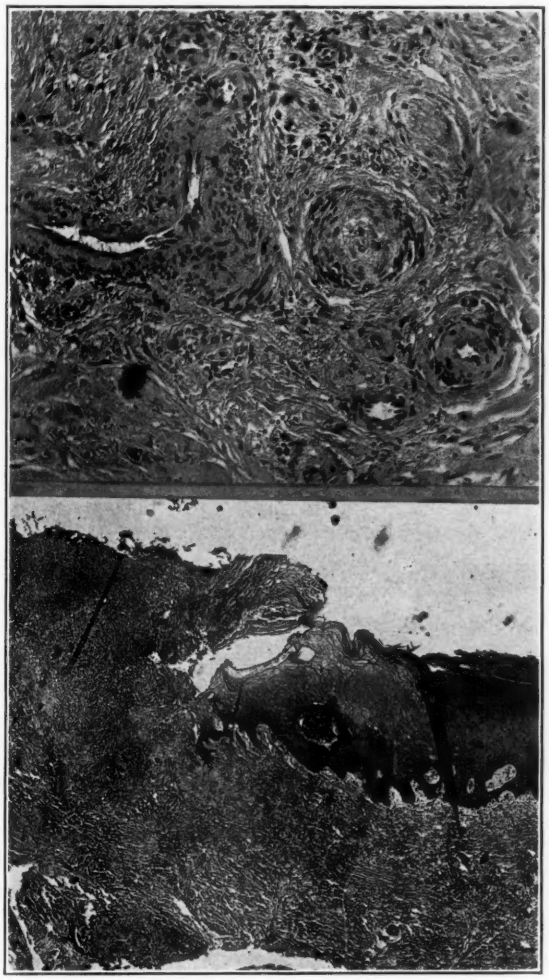


Fig. 1*C*.—See opposite page for legend.

exposure, the susceptibility of the skin increases and a chronic dermatitis develops. Pullinger has shown experimentally that the effects resemble those of inflammation. There is first a stage of hyperemia, which, if sufficiently severe, is followed by exudation, extravasation of blood, and thrombosis. While her study was not made with reference to chronic irradiation dermatitis, the importance of vascular injury is apparent.

The dermatitis and carcinoma which follow repeated minimal adventitious exposures to x-rays are characterized by latency and multiplicity (Figs. 1-3). The dermatitis does not develop immediately after the initial exposures, but months or even years may elapse before the keratoses and telangiectases appear. They do not necessarily become malignant, and, if exposure is avoided not only to roentgen and radium irradiation but to excessive sunlight and possibly even to irritant chemicals as well, the lesions may remain stationary and the hands may be kept fairly comfortable by the use of bland creams. Usually, however, once started the keratosis and dyskeratosis do not disappear and new areas develop in previously normal appearing skin. Then,

Fig. 2.—Early epidermoid carcinoma on dorsum of left hand in a 52-year-old physician. (P.M.H. 14703, 1933.) In 1918 the hand was exposed to a considerable dose of x-ray irradiation and a few months later an ulcer developed, which persisted without pain or increase in size for five years, at which time the hand became quite scaly. Both the ulcer and the scaliness have remained unchanged for some thirteen years. The ulcer was excised, a free full-thickness graft applied, and healing occurred without reaction. Microscopic study of the ulcer showed considerable inflammatory hyperplasia of the skin, irregular branching masses of epithelial cells with numerous mitoses, and marked diminution of vascular supply.

especially if further exposure takes place or if unwise treatment is given, changes occur which we recognize as cancerous or as precancerous. There appear painful cracks or ulcers which become infected and heal with great difficulty. Some may never heal or the same area may repeatedly break down, finally to form a progressively enlarging persistent ulcer. Such an ulcer may prove to be a carcinoma, but it rarely recurs following excision. However, a succession of such keratotic areas may break down, ulcerate, and become malignant, and it

A.

B. *C.*

Fig. 3.—*A*, Roentgen dermatitis and carcinoma with history extending over a period of twenty-eight years. Hyperkeratosis had started fifteen years previously following x-ray irradiation, and one year previously (1924) an ulcer had developed on the middle finger, numerous areas of hyperkeratosis over the dorsum of the hand, and an enlarged axillary node. The finger was amputated and the axilla was dissected; carcinoma was found in both places. *B*, Photomicrograph of the squamous cell carcinoma of the middle finger. *C*, Photomicrograph of the carcinoma metastasis in an axillary node.

is this chronicity and the multiplicity of malignant lesions which characterize irradiation dermatitis and give the clue to treatment.

The tendency in the treatment of irradiation carcinoma is frequently too conservative in that, while the ulcerating lesions are removed, large areas of keratotic skin are left behind. It should be remembered that the damage is extensively scattered over the dorsum of the hand and fingers, that not one lesion but from two to twenty or more may develop into carcinoma, and that malignancies developing subsequent to excision are not recurrences but new lesions. All damaged skin should be removed, preferably in one stage regardless of the extent of the actually malignant area (Figs. 3*E* and 3*K*). Tiny keratoses often may be individually excised or desiccated, and where there are

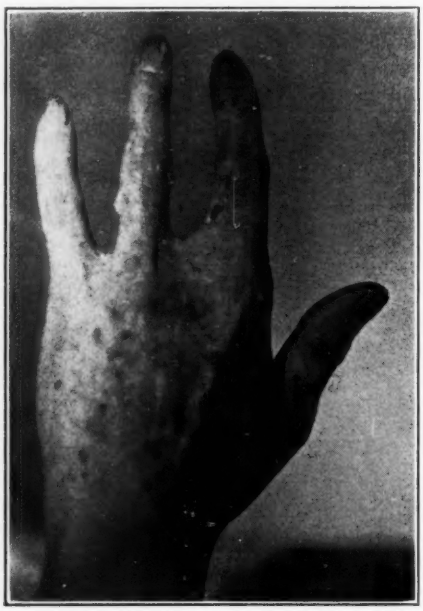


Fig. 3*D*.—The patient returned in 1931 for treatment of numerous areas of keratosis and ulceration of the same hand.

but few such areas and considerable normal appearing intervening skin individual removal may be satisfactory. If the disease is extensive, it is necessary to remove practically all of the skin from the dorsum of the hand and fingers.

The removal of a large amount of skin from the hand entails the covering of the raw surface. Some surgeons have advocated a delayed skin graft, preferring to allow the raw surface to become covered with clean granulations before applying a graft. It is my feeling, however, that an immediate graft can be applied if sufficient pains have been taken beforehand to clean the skin and minimize the always present infection. It is our practice to hospitalize the patient for several days or a week preceding operation and during this time, by

frequent changes of dressings and scrupulous cleanliness, to reduce the infection and contamination of the surface.

There is some choice as to the type of graft to be used, depending on the area to be covered and the nature of the raw surface. Following removal of small areas of skin where there is no infection and where tendons are not exposed, a free full thickness graft may be applied. For larger areas the graft of intermediate thickness of Blair and Brown is very useful (Fig. 1). In instances in which sub-

Fig. 3*E*.—Because of the extensive involvement, the skin over the dorsum was excised in toto.

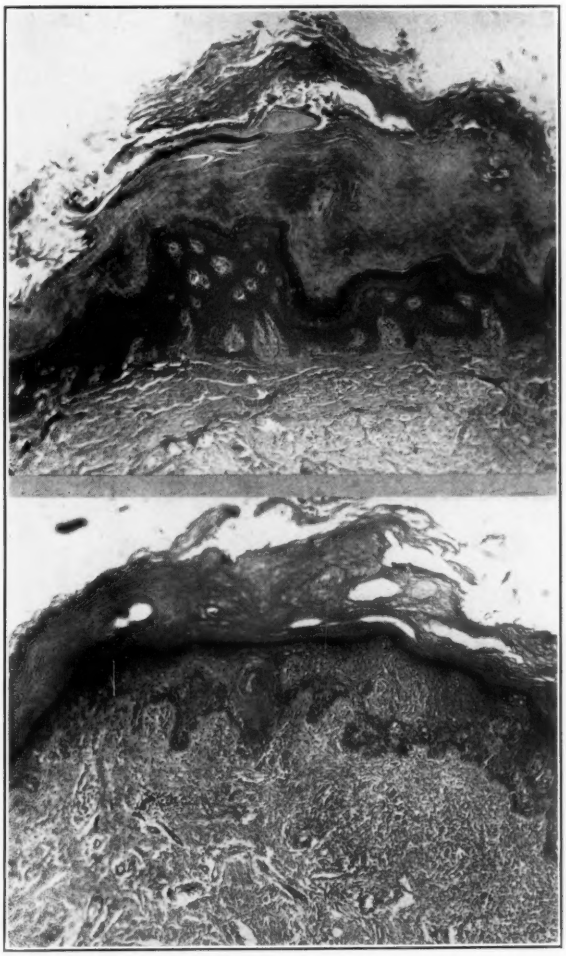
cutaneous fat is needed, a pedunculated flap or pocket flap is indicated (Fig. 3*F*).

There is some difference of opinion as to the logical management of the regional lymph nodes. Handley advises radical removal of the epitrochlear and axillary nodes in every case of roentgen carcinoma, regardless of the extent. He also excises the strip of fascia which lies over the medial intermuscular septum and contains the important lymphatic vessels connecting the two groups of nodes, and he states

F.

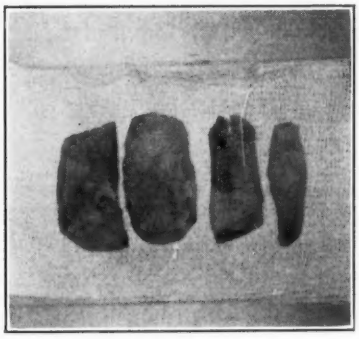
G.

Fig. 3.—*F*, The hand was placed in a pocket flap on the thigh, where it remained for one month. *G*, The flap healed satisfactorily and in November, 1930, the patient had regained good use of the hand. (In 1934 following exposure on a hunting trip the flap broke down along the radial border on the index finger and this was excised and a small pedunculated flap applied.)



H.

I.



J.

Fig. 3.—*H*, In June, 1930, areas of keratosis excised from the right hand showed beginning basal cell carcinomas. *I*, In August, 1931, a warty growth excised from the left forearm showed early epidermoid carcinoma. *J*, In June, 1934, the patient returned for further treatment of persistent areas of hyperkeratosis on the dorsal surfaces of the fingers of the right hand.

that this operation is a safeguard in case carcinoma develops in subsequent lesions. Blair believes that gland dissection should be performed if the lesion is deep. It is my feeling that in the case of superficial lesions without palpable nodes in which excision of the skin is all that is necessary to remove the diseased areas the glands may be left alone. If, however, it is necessary to amputate fingers, if the lesion has penetrated into the deep fascial planes, tendons, or bones, if palpable nodes are present, an axillary and epitrochlear dissection should be carried out.

Fig. 3*K*.—These areas were all excised and microscopic examination revealed marked inflammatory hyperplasia of the skin, the so-called precancerous stage.

The use of any type of irradiation is absolutely contraindicated. Even the mild exposure to ultra-violet irradiation which is sustained on a golf course may occasion great discomfort to a patient with an "x-ray hand." It would hardly seem necessary to caution against the use of radium or x-ray were it not that these agents are so frequently employed. In the early stages of the dermatitis before the real nature of the lesion is recognized, irradiation, while possibly excusable, may lead to serious trouble. There is no justification how-

ever for roentgen or radium therapy after the true nature of the condition is known.

The prognosis of roentgen carcinoma depends upon the stage it has reached before operative care is given; although they are squamous cell carcinomas, they tend to develop slowly, metastasize late, and there is adequate time for complete eradication. Too often, however, temporizing procedures are tried; there is further exposure to x-rays, and new lesions develop from time to time in regions of the hand not at first seriously involved. If it is remembered that all of the dry keratotic skin on the dorsum of hand and fingers is potentially malignant, wider excisions will be done and fewer recurrences and metastases will occur. The prognosis is not necessarily unfavorable even if the glands are invaded, though admittedly it is not so good. In the case illustrated in Fig. 3 despite axillary metastasis and the subsequent development of other areas of carcinoma on the hand the process did not become generalized, even after some thirteen years.

Carcinoma also may develop on the basis of radium dermatitis but by no means so frequently as in roentgen dermatitis, possibly because radium was introduced later than x-ray and its dangers were realized. I have seen several instances of radium dermatitis, but I have never seen a carcinoma on the basis of chronic radium dermatitis. Such cases have been reported (Wakeley, 1927) and the pathogenesis and pathologic picture appear to be the same as for roentgen carcinoma.

Solar irradiation probably plays an important role in the development of carcinoma of the dorsum of the hand in sailors, farmers, and others whose hands are exposed to wind and weather for long periods of time. The keratoses which appear in old people are also probably the result of these same influences and it is not always certain how much significance is to be attached to the different types of irritation, sun, wind, mechanical irritants, and the lowered vitality of aged skin. The irritating property of sunlight to skins already afflicted with roentgen dermatitis is well recognized.

Carcinoma of the extremities following exposure to chemicals is found chiefly on the hands of persons exposed to tar, grease, gasoline, oil, and paint. Adair believes this type of occupational carcinoma is on the increase, that service station employees are especially liable to develop it, and that the danger is especially great in the case of a combination of chemical and mechanical trauma. Ligge, who has studied the problem of occupational dermatitis and carcinoma in industry in Great Britain, has found that workers exposed to pitch, tar, paraffin, mineral oil, and their derivatives show a high incidence of cutaneous carcinoma. Briquette workers and cotton-mule spinners develop carcinoma as the result of exposure of the skin to irritant chemical oils, especially certain types of mineral oil. Ligge found in 123 cases of carcinoma among briquette workers 9 involving the hand; and of

1,062 cases of carcinoma in cotton-mule spinners, who are exposed to mineral oil spray from the spindles, 70 per cent involved the scrotum and 30 per cent the hands, arms, and other parts of the body. The Public Health Bulletin No. 215, in reporting upon the skin hazards in American industry, found 12 cases of carcinoma among 4,507 workers in the oil and wax industry; of these, 2 were on the hand.

Arsenic is the only internal medication which appears to cause carcinoma of the skin. The majority of patients with arsenical dermatitis give a history of having continued the use of Fowler's solution on their own responsibility for many years after it had been prescribed. The first lesions occur typically as patches of hyperkeratosis and scaling on the palms and soles, but as the disease progresses more and more of the body surface is involved until finally most of the skin of the body is affected. Malignancy may develop in any of the cutaneous lesions and makes itself manifest by the appearance of cracks and ulceration in areas of keratosis. Pain seems to be a rather typical feature of this carcinoma. In common with irradiation carcinoma malignancy may occur in more than one of the areas of arsenical keratosis. The prognosis is bad probably because the chronic nature of the lesions leads to neglect in seeking treatment and because of the development of multiple malignancies.

Chronic mechanical trauma does not appear to be very frequently the cause of carcinoma of the extremities. Although Volkmann recorded one case developing on the basis of an ingrown toenail, the case appears to be unique despite the great frequency of this supposedly causative factor. Most reports of cases of carcinoma ascribed to mechanical trauma consist of single case records. The rarity of carcinoma in corns and calluses minimizes the importance of chronic mechanical trauma, certainly when acting alone.

Carcinoma may occur in cutaneous scars, particularly those resulting from burns (Treves and Pack), the "Marjolin ulcer." The burn scar is the most frequent single definite factor in the development of carcinoma of the extremities. A striking characteristic of the burn scar is the long duration before carcinoma develops. In a collected series of burn scar carcinomas of the hand the average duration of the scar before the onset of malignancy was found to be 43.3 years, the oldest scar being 66.5 years and the youngest 3 months. The factors which lead to the occurrence of carcinoma in a burn scar are not clearly understood; in fact, there are some who doubt the validity of the term "burn scar carcinoma." However, it occurs with sufficient frequency and is present so often in carcinoma of the extremities that it must be seriously considered. The factors in burn scar which appear to predispose to the development of cutaneous carcinoma are probably two: vascular and traumatic. The thin skin which covers the thick avascular fibrous scar is poorly nourished and easily traumatized, both because of its elevated position and the thick hard tissue over

which it lies. There are some who believe that the carcinoma develops from epithelial cells which have been displaced and lie in the connective tissues of the scar. These cells following nutritional disturbance and trauma are thought to be the ones which undergo carcinomatous proliferation.

The active lupus lesion or the lupus scar appears to be a site for the development of carcinoma with sufficient frequency that the lupus carcinoma has come to be a clinical entity. According to Mündelein's statistics, 3.2 per cent of all cases of lupus develop carcinoma. In 2,575 cases he found 83 with carcinoma; of these 5 occurred on the extremities, 4 on the upper and 1 on the lower. There is no agreement as to the factors leading to the development of carcinoma in lupus. The lupus itself, the long-continued epithelial proliferation which it produces, and the constant irritation of medicaments used in treatment have been suggested as possibilities. Roentgen irradiation has been accorded a prominent place and some have suggested that since the advent of roentgen treatment lupus carcinoma has increased. This assertion, however, has not been definitely proved (Mündelein).

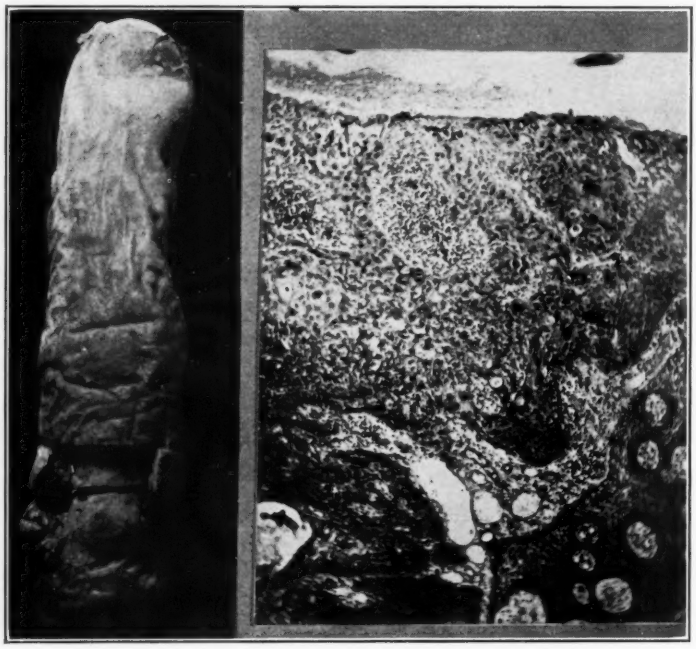
Other types of chronic inflammatory processes may lead to the development of carcinoma. Draining sinuses of various types and chronic nonspecific ulceration may eventually become malignant. Carcinoma may develop in osteomyelitic sinuses; the epithelial proliferation may occur in skin which has grown into the sinus from the surface; and the bone may be the seat of a primary epithelial neoplasm and the carcinoma may go unrecognized for a long period of time. Carcinoma develops very rarely in chronic varicose ulcers. Tenopyr and Silverman analyzed 1,000 cases of chronic ulcers of the leg and found but 14 cases of malignancy. Of these, some 4 appeared to have developed on the basis of a varicose ulcer; 5 apparently were primary carcinomas of the skin; 2 were ulcers of less than two years' duration (and were considered primary); 1 occurred in an osteomyelitis wound; 1, in a compound fracture; and 1, in a burn scar. They cite the literature and note especially the work of Knox (1925), who was able to collect 59 instances of carcinoma of the leg, about one-half of which seemed to have developed on the basis of ulcer. Chronic paronychia (Silverman) is occasionally the basis for the development of an epithelioma.

Chronic ulceration and carcinoma sometimes follow a single injury and in such instances it is difficult to decide if the injury or the subsequent infection is the etiologic factor (Fig. 4). Among such single injuries which have preceded the development of carcinoma are various types of puncture wounds, animal bites, and crushing injuries to the nail bed. Duhot, Layne and Delacourt have briefly reported an instance of carcinoma of the hand which followed a puncture wound with copper wire and note six other similar cases in their report. In the present state of our knowledge it is not possible to be dogmatic about the possibility of the development of carcinoma following a

single trauma. It has never been experimentally produced and in such cases as are reported the data are often insufficient to warrant a definite conclusion.

Various other lesions (furuncles, carbuncles, and pellagrous dermatitis) have been given as precursors of carcinoma on the hand.

Carcinoma may develop on the basis of some previous skin tumor and in such instances there is always the question whether the lesion has not been malignant from the start (Highman). The previously present neoplasms may have been congenital tumors or they may have appeared some time in later life. Carcinomas appearing in congenital neoplasms are quite rare, but their invariably malignant course puts them in a group by themselves.



A. *B.*

Fig. 4.—*A*, Subungual carcinoma of nail bed, left little finger, which followed a severe crushing injury nine months previously. The wound became badly infected and was treated elsewhere with salves and ointments without success. The finger became extremely painful and the patient applied to the Northwestern University Clinics, where amputation was performed by Dr. Hart. There had been no recurrence one year later. *B*, Photomicrograph of microscopic section shows a squamous cell carcinoma of the nail bed.

Those carcinomas arising in cutaneous warts and nevi which appear in later life usually present a history of some sort of trauma, either accidental or in attempts at self-treatment (Figs. 5 and 6). Not infrequently a cutaneous wart has been treated by irradiation, salves, and incomplete excision each time with prompt recurrence. Such lesions have a worse prognosis than do tumors originating on an irritative basis only; not so bad, however, as do carcinomas occurring in congenital neoplasms. Whatever our opinion may be concerning the origin of the carcinomas, whether or not it appears logical to assume

that some benign neoplasm has undergone so-called malignant degeneration, the fact remains that this group of carcinomas is the most malignant of all of those of the hand.

Occasionally the skin has been normal until the neoplasm developed; there is no history of any irritation, no scar or chronic infection, irradiation or previous neoplasm.

A few general etiologic factors are of some interest. The average age of 239 cases of carcinoma of the hand was found to be 59 years, with practically the same average for each sex. It does not appear to hold true that carcinoma of the hand develops at a more youthful age when it occurs in a congenital neoplasm than when some irritative factor is present.

Males outnumber females almost 2 to 1 and in the chronic irritation group slightly over 2 to 1; whereas, the roentgen carcinoma occurs almost exclusively in males. Carcinoma of the hand is often spoken of as carcinoma of the dorsum because of its most frequent location. Except in the case of roentgen carcinoma, the right side is more often attacked than the left in a ratio of slightly less than 2 to 1. However, of those cases in which the tumor developed from apparently normal skin, the ratio in 25 cases was 12 right to 13 left.

Carcinomas of the hand are usually characterized by a long chronic course. As a rule an ulcer has been present for from one or two years before the condition is diagnosed as carcinoma and it is logical to assume that it has actually been malignant for most of that time. For convenience of description the clinical course may be divided into the preulcerative and the ulcerative stages. The lesion usually starts as an indurated nodule or as a scaly symptomless tumor, the surface of which may be thin, dry, and parchment-like or hypertrophic with gray or reddish papillary projections from its surface and surrounded by dilated capillaries. Such lesions may persist without causing disturbance for many years and then break down, spontaneously or after trauma. Cracks may appear which refuse to heal or crusts may form which upon being removed leave a thin, red, shiny or ulcerated surface. There then develops an ulcer or an irregular granular cauliflower-like mass.

The ulcer or cauliflower growth enlarges slowly, involving first the neighboring skin and subcutaneous tissues. It may attain quite sizable dimensions before the deeper structures are actually invaded. Tendon, bone, and muscles, however, eventually are involved, although this may not occur until quite late. As the tumor develops, it becomes infected and necrotic; a seropurulent or serosanguineous discharge appears, often very malodorous. Occasionally hemorrhage takes place and may be quite severe.

Involvement of the lymph glands comes late, often not for two years or more after the ulceration. Of 122 collected cases in which

information was given, glandular enlargement was present in 62 and absent in 60. The mere presence of enlarged lymph nodes does not connote metastasis since it is often the infection which is accountable. If, however, the nodes are enlarged, they should be considered to be malignant until proved otherwise.

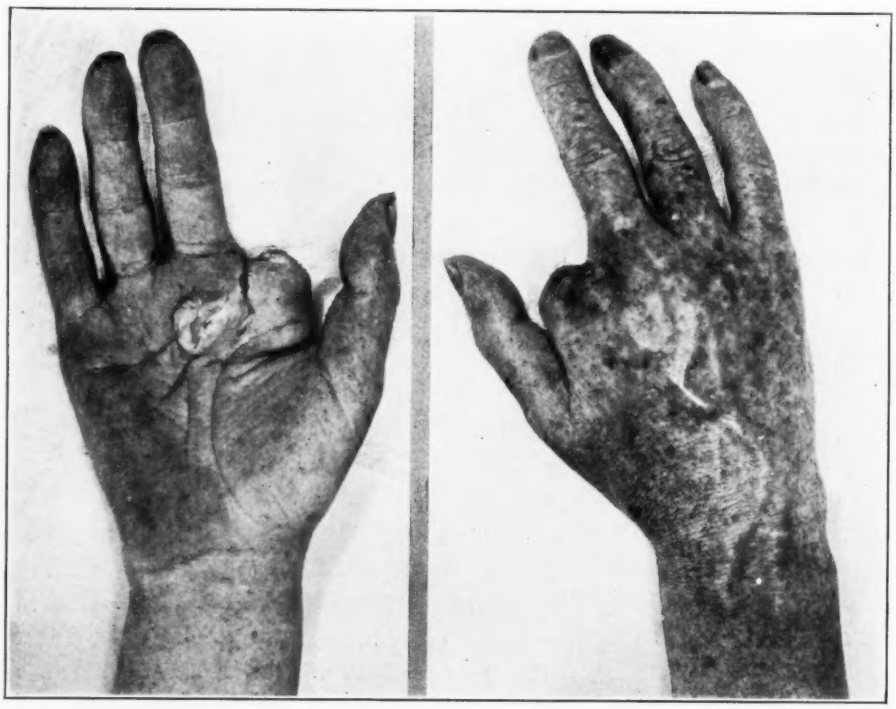


Fig. 5.—(P.M.H. 4771.) Squamous cell carcinomas of right hand in a 42-year-old wool handler. In January, 1934, a small wartlike growth appeared on the dorsum of the distal interphalangeal joint of the index finger. He treated this himself for some six months with sulfuric acid and hot needles without success and finally consulted a physician in June, 1934. There was a most peculiar odor to the discharge at this time and hot boric dressings were applied without results for several weeks. He consulted a second doctor, who snipped off the lesion with scissors and sent the patient to a dermatologist. The small ulcer then present was treated with radium and x-ray, following which a slough developed which left a deep infected ulcer for which the finger was amputated at the proximal interphalangeal joint. The operative wound became infected and a sinus developed between the distal end of the stump and the palm. This was treated as an infection for somewhat over a year, at which time, because of the unbearable pain the patient consulted another surgeon who amputated the stump at the metacarpophalangeal joint. Two months later the pain and swelling recurred and a granulomatous ulcer with a foul-smelling discharge developed in the palm. Biopsy and cultural studies having failed to afford a diagnosis, the patient was given potassium iodide for several months without relief. At time he was first seen, somewhat over two and one-half years after the development of the "wart," the cultures were not significant, but a biopsy revealed an ulcerated squamous cell carcinoma. The hand was amputated through the middle of the forearm in September, 1936, and enlarged axillary lymph nodes dissected out. No metastases were found in the nodes. There has been no recurrence up to December, 1938.

The terminal symptoms are due to the local destructive action of the growth, infection, and occasionally to generalized metastases. Pressure on the brachial plexus by enlarged axillary and cervical nodes may cause excruciating pain which often can be controlled only by nerve section or chordotomy. Toxic absorption or sepsis from the local growth may be overwhelming. Generalized metastases to the

parenchymatous organs, especially the lungs and liver, are of late occurrence.

The pathologic picture does not differ from that of carcinoma elsewhere on the skin. The majority on the hand are squamous cell in character, a very few are basal cell, and an occasional one transitional or basal squamous carcinoma. A basal cell epithelioma may become a squamous or basal squamous type, and when a basal cell lesion recurs following treatment this transition frequently will be found to have taken place. If a system of grading is followed, 90 to 95 per cent of the tumors will be found to fall into Groups I and II of Broders' classification (DeBell and Stevenson) and only the rare one in Group III and still more rarely in Group IV.

Fig. 6.—Thick split graft applied to surface left by excision of an early squamous cell carcinoma of dorsum of hand (P.M.H. 27107, 1936). The patient, a 72-year-old farmer, noted a wart or pimple on the dorsum of his hand some fifteen to sixteen years previous to admission. The wart came off and a crust formed over the resultant ulcer. For a number of years the ulcer slowly enlarged, crusting over from time to time until finally a purulent discharge developed. The application of various salves and the use of acids did not retard the growth and in 1932-33 eight or ten x-ray treatments were given without benefit. In May, 1934, he was operated upon elsewhere: the area was excised and a skin graft applied. This "took" at first but eventually broke down and the following year ten more x-ray treatments were given. In July, 1936, the ulcer was widely excised by Dr. S. L. Koch and a thick split graft applied. This has remained healed to date.

The diagnosis of carcinoma is made on the gross appearance, substantiated by microscopic sections. The development of malignancy in the brown, dry, scaly keratoses in elderly persons, farmers, sailors, and others exposed to wind, rain, and sun is suggested by induration and a mild inflammatory reaction. In physicians who have been exposed to roentgen irradiation, the presence of hyperkeratoses and ulcers at once suggests the possibility of carcinoma. The exuberant cauliflower-like growths may suggest a granuloma, but cultures and biopsy should make the diagnosis certain. Stubborn lesions of the

nail bed which resemble paronychia may be treated for some time as chronic infections before the true nature of the condition is suspected and proved by microscopic section. Bick has emphasized the occurrence of pain in an ulcer or sinus after a period of quiescence as suggestive of the onset of malignancy.

The prognosis on the whole is relatively good, because of the long slow course of the disease before extension and metastasis occur. However, the carcinoma is invasive and produces lymph node and organic metastases if not removed, and the prognosis depends upon the stage at which the lesion comes under adequate treatment, on the presence of lymph node involvement, infection, multiplicity of lesions, etc. In a study of 134 cases (exclusive of roentgen carcinoma) of all stages a favorable outcome was found to be reported in 65 per cent. When we begin to break down the statistics according to etiologic factors, we find that the best prognosis is offered by those cases in which the carcinoma arose on previously normal skin without any known preceding factor. The next best prognosis is in those cases in which the carcinoma followed some of the various irritative lesions noted above. Carcinoma arising from a previously present neoplasm or wart presents the worst prognosis and if the original neoplasm has been congenital the outlook is as bad as for the malignant melanomas.

Despite the rarity of metastases, the prognosis for lupus carcinoma is not favorable. Of Mündelein's 83 cases, 39 died of their carcinoma, 4 were inoperable, and 8 refused treatment. Of the remaining 42 patients, 14 only were free of recurrence at the time of his report and of those only 3 had been under observation for five years or over.

The presence of lymph node involvement, whether this be proved to be due to carcinoma or not, definitely impairs the prognosis. While the presence of enlarged lymph nodes does not prove that metastases are present, the absence of lymph node enlargement is rather good evidence that there is no metastasis. In no recorded instances in which the glands were not palpable before operation and were dissected out were they found to be invaded. DeBell and Stevenson have made the same observation. When glandular enlargement is present, there is failure to obtain successful result in nearly 60 per cent, while if glands are not present this figure is reduced to 25 per cent.

The treatment of the isolated lesion will depend upon its extent. It is my feeling that surgical removal is to be preferred to diathermy or cautery destruction, and in this I agree with DeBell and Stevenson. The small lesions on the dorsum of the hand usually can be excised and the resultant defect sutured. It is seldom possible, however, to excise lesions on a finger and close the defect by suturing since the skin here cannot be sufficiently relaxed and often even small excisions must be closed with a graft. Large carcinomas which have remained

superficial usually may be completely excised and the defect immediately repaired with a graft of intermediate thickness. Here, as in roentgen carcinomas, a careful preparation of the hand is necessary in order to reduce the ever-present surface infection to a minimum. If excision of the tumor has exposed tendon and bone, a pedunculated flap is needed and again the pocket flap will be found to be the most useful.

Although irradiation is extensively used in the treatment of cutaneous carcinoma, it is my feeling that those of the extremity are best treated by excision. The extensive necrosis with exposure and destruction of tendon and bone which are liable to follow therapeutic irradiation of the hand renders it unsuitable in any but the smallest lesions. Burn scar carcinoma, already situated in poorly vascularized tissue, should not be subjected to irradiation.

Deep ulcerating carcinomas and large fungating masses may be so extensive that very mutilating procedures will be needed if local excision is performed. The surgeon must carefully weigh the possibility of sparing a sufficient amount of tissue to leave the patient a functional hand against the possibility of insufficient removal of malignant tissue. Amputation of the extremity occasionally must be practiced, and, because of the ever-present infection both in the local tumor and in the lymphatics of the forearm and arm, primary healing of the stump may not occur. In case of carcinoma of the nail bed it is usually advisable to amputate the digit. These lesions are prone to be very malignant and an occasional one turns out to be a melanoma.

The same procedure with reference to lymph nodes should be followed here as in roentgen carcinoma. If the nodes are not palpable, it is very doubtful if they are invaded; if they are enlarged, the chances are 50 per cent that metastases are present. Enlarged nodes, of course, should be removed, while if the primary lesion is deep and invasive and if amputation is necessary a dissection of the axillary and epitrochlear glands should be practiced.

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SUBUNGUAL MELANOMA*

The Differential Diagnosis of Tumors of the Nail Bed

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In 1886 Jonathan Hutchinson described melanomas of the nail bed, to which he applied the term melanotic whitlow. In explanation of this nomenclature, Hutchinson said: "Because it resembles whitlow and is usually so named at first, I prefer to give it that name." The same lesion has been designated by various synonyms, such as onychial melanoma, subungual melanoma, and melanocarcinoma, melanosarcoma, or melanoblastoma of the nail bed. This regional occurrence of melanomas provides an interesting clinical study.

Subungual melanoma is rare in comparison with other diseases of the nail. Pardo-Costello found only 1 subungual melanoma among 94 patients with nail diseases seen during a period of six months. White found no melanomas among 485 patients with nail diseases treated during three years at the Massachusetts General Hospital and in private practice.

A small proportion of melanomas are subungual in location. In 1932 Farrell reported on 265 cases of melanoma, 6 of which were subungual; and Affleck, in 1936, found the same number in a total of 266 cases. In a report published from the Memorial Hospital in 1930, there were 4 subungual melanomas in 218 melanomas of all locations. Continuing this report through the year 1937, to cover the twenty-one years since 1917, our figures show 477 cases of melanoma. The 16 subungual melanomas represent 3.4 per cent of the total.

The average age of our patients with melanomas of various regions was 47.9 years. For the patients with subungual melanoma it was somewhat higher, namely 58.7 years. This is consistent with the data available for 48 of the cases reported in the literature, their average age being 55.9 years. For our group the range was from 30 to 71 years; for the reported cases, from 23 to 80 years.

The sex was given for only 55 of the reported cases, 26 males and 29 females. In our series there were 10 males and 6 females. Of the total cases, therefore, slightly more than one-half were males.

The frequency with which the various digits are the site of subungual melanoma is shown in Table I.

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TABLE I

SITE	TOTAL CASES		REPORTED CASES		MEMORIAL HOSPITAL CASES	
Total		85		69		16
Hand (total)		48		38		10
Thumb	27		22		5	
Finger	19		14		5	
Not specified	2		2			
Foot (total)		37		31		6
Great toe	34		30		4	
Toe	3		1		2	

Of the subungual melanomas reported in the literature, the great toe was the most frequent site, with 30 cases, followed by twenty-two located on the thumb. In our experience they are more frequent on the hand.

Melanoma in general is more common on the foot than on the hand. Of our 477 cases of melanomas of all locations, 74, or 15.5 per cent, were located on the foot, with the 6 subungual melanomas, 8.1 per cent, of the 74. Only 29 of the 477 tumors, or 6.1 per cent, occurred on the hand, with 34.5 per cent of these subungual in location.

Melanomas are comparatively rare in the negro, with the exception of certain reports from Africa. Thirty-four have been reported in the literature, excluding the African natives. Melanomas in negroes tend to develop in those parts of the body which contain the least pigment; e.g., on the soles of the feet. The matrix of the nails in negroes is not so deeply pigmented as the skin, which is significant in view of the relative frequency of subungual occurrence. There were 7 negroes in our series of 477 cases, only 1 of whom had a subungual melanoma, located on the thumb. Bauer reported 2 cases of subungual melanoma in negroes, 1 on the thumb and 1 on the great toe; Dickson and Jarman, 1 on the finger; and Hewer, reporting on 47 melanomas seen in Khartoum in the five years from 1929 to 1934, found 2 cases occurring in the nails of the fingers.

A consideration of the anatomy of the nails is of interest before discussion of the clinical appearance of subungual melanoma. The nail and nail bed are epidermal and dermal appendages very much like the hair follicle in genesis. The nail is the analogue of hair; and the nail matrix, of the germinative layer of the hair follicle. The follicle in primitive animals is a tactile end organ with abundant nerve supply; the nail bed also is exquisitely sensitive and contains numerous tactile end organs. Some of these are involved in the genesis of melanoma, which is essentially a tumor of the end-organ apparatus. As will be mentioned later, the glomus is another peculiar structure found in the nail bed which may undergo neoplastic changes. The nail matrix is the only reproductive portion of the nail and it bears a close morphologic resemblance to the stratum malpighii of the skin. The hyperkeratotic nail plate overlies the nail bed, the epithelial

layer of which is continuous with the matrix. The nail bed plays no role in the formation of the nail plate, but it is a corium rich in nerves and blood vessels, which are important in maintaining the nutrition of the nail.

Hutchinson's description of the appearance and behavior of these so-called melanotic whitlows is well worth quoting: "It needs sometimes the eye of faith to recognize the narrow band of black which borders the inflamed part. It would seem that the power to produce a pigmented structure is but feeble in the neighborhood of the nails; whenever there is much growth, a nonpigmented mass is produced. The mixture of colored and uncolored growth in melanotic sarcoma is of course common in all parts, but in none is it, I think, so marked

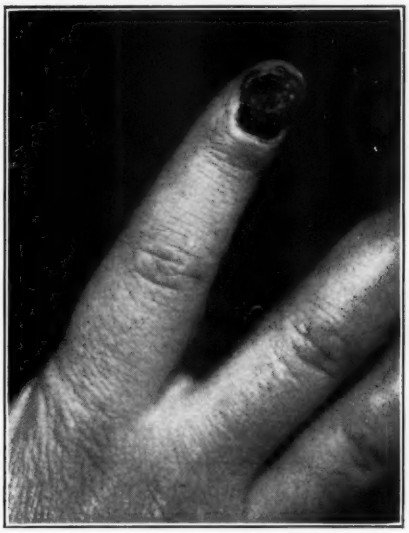


Fig. 1.—Subungual melanoma. Note the pathognomonic border or halo of black pigment at the edge of the involved nail.

as in the proximity of the nails. The disease is slower in its stages than is the case with melanosis in most other positions. So far as I know, the growth presents no histologic peculiarities. Yet there is much greater hope of delaying the progress of the disease by operation than exists in most other forms of melanosis."

The fully developed lesion is usually a black, fungating, well-demarcated ulcer, involving the nail sulcus and matrix and elevating the nail. The nail itself becomes thickened, brittle, split, and finally ulcerated. The melanoma sometimes has the appearance of purplish granulation tissue, flecked with small areas of scattered black pigment. A pathognomonic point in diagnosis is a border of coal black color which is nearly always present at the edge of the involved nail (Fig. 1). An important point concerning the early gross appearance is the fact that the tumor seems to be independent of the skin, grow-

ing from beneath, displacing, and elevating the eponychium. In the early stages the surface epithelium is intact. About the time of ulceration, pigmented streaks often appear in the skin surrounding the tumor. From the ulcerated surface a thin dark fluid exudes which stains the dressings and becomes brown, like melanotic urine on exposure to air. The local lesion is limited in the direct extension of its growth by the fascial planes of the distal phalanx in a manner similar to that seen in infections. The melanoma begins in the nail sulcus more frequently than in the middle of the nail bed.

The predominant cells of these subungual melanomas are of two types: (a) the fusiform spindle cells, with hyperchromatic nuclei, intra- and extracellular pigment, and infrequent mitoses (the melanoma of this histologic variety is frequently called melanosarcoma); (b) the spherical, polygonal, or epitheloid cells, often in sheets and pseudoalveolar arrangement, with less pigment and more frequent mitoses (the melanoma of this histologic variety is often termed melanocarcinoma). Regardless of the histologic picture and cell type, all the subungual melanomas pursue the same clinical course and metastasize by way of the lymphatic vessels to the regional lymph nodes. The melanoma cell emboli usually skip the cubital and popliteal lymph nodes to lodge in the axillary and inguinal lymph nodes. The metastatic tumors frequently are darker than the primary melanomas of the nail bed.

A pigmented spot under the nail may remain quiescent for a long time, as is characteristic of pigmented naevi in other parts of the body. In Boyer's patient it was inactive for twenty-eight years. The onset of true melanoma may be a slow insidious development, but once the tumor begins to grow and assert its malignant properties, the ensuing course may be fairly rapid. Pain is never conspicuous, even as a late symptom.

DIFFERENTIAL DIAGNOSIS

The most important problem concerning subungual melanomas is the correct early diagnosis. Failure to diagnose correctly frequently may mean that the favorable time for operation has passed. Many patients are at first treated for infection. An examination of the blood is of no help, and black coloration of the urine is a late phenomenon. In general, the subungual melanomas may be differentiated from benign tumors in that the latter do not break through the nail. It is essential to distinguish this tumor from the following pathologic lesions of the same location:

1. *Paronychia; Whitlow or Felon; Osteomyelitis.*—The age of the patient, antecedent history, absence of pigmentation, acute onset, acute tenderness, pain, redness, purulent discharge, and rapid course are

features of these infections which serve to differentiate them from melanoma. If melanotic whitlow is unrecognized and the treatment is the same as for paronychia, a fungating lesion soon develops, with loss of the nail and invasion of the regional lymph nodes. Chronic osteomyelitis secondary to or independent of felon may so disturb the appearance of the nail and nail bed as to simulate a neoplasm (Fig. 2). Lateral roentgenograms of the terminal phalanx should be made in the case of all subungual tumors.

2. *Pyogenic Granuloma.*—The simple papillary granuloma is of frequent occurrence about the nail sulci (Fig. 3). It is soft and extremely

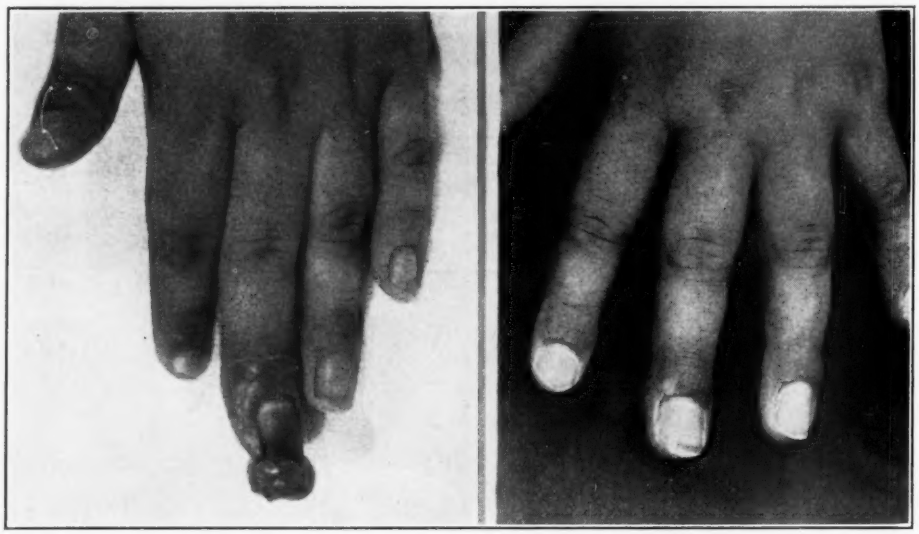
Fig. 2.—Osteomyelitis of terminal phalanx simulating subungual melanoma.

vascular. There is an abrupt, sharp, punched-out line of demarcation between the tumor and the skin which surrounds it. It grows rapidly, recurs usually after attempted surgical removal, and disappears, as if by magic, following the application of a small dose of roentgen-ray or radium therapy. Its radiosensitivity, evolution, and appearance are points of diagnostic importance.

Case Report.—E. S., a 9½-year-old girl. A small subungual wart on the end of her finger became infected when she squeezed it. It increased in size and involved the distal phalanx of her finger (Fig. 3). A roentgenogram at another hopsital was negative for osteomyelitis.

Low voltage x-ray therapy, 1,500 r. units, in one dose was given to the finger with good results.

3. *Onychomycosis Nigrescens.*—A parasitic fungus of the ringworm family which occasionally involves the nail and matrix. Because of the production of black pigment, it is easily mistaken for subungual mela-



A. *B.*

Fig. 3.—*A*, Pyogenic granuloma before radiation therapy; *B*, pyogenic granuloma after radiation therapy.

Fig. 4.—Case 10. Moulage of hand showing subungual melanoma. A black pigment-producing fungus was isolated from scrapings of this nail.

noma. Microscopic examination of the nail scrapings dissolved in potassium hydroxide solution reveals the presence of the fungus in a certain number of cases. Subungual melanoma involves only one nail bed,

whereas onychomycosis generally is distributed about other nails of the same hand or foot. The two diseases may be coexistent, since ringworm of the nails is such a common infection (Fig. 4, Case 10).

4. *Subungual Hematoma.*—A black or brown melanotic spot under the transparent nail may resemble the black ecchymotic area of old extravasated blood following an injury. The importance of the differential diagnosis in this instance lies in the fact that hematomas of the nail bed are common and trauma seems to be an occasional inciting factor in subungual melanomas. The definite history of antecedent trauma, the color changes characteristic of a bruise, and the suffusion of blood into the surrounding integument identify the lesion as a hematoma. Under the mistaken diagnosis of subungual hematoma, surgeons have drilled holes through the nail plate in order to evacuate supposed blood clot, only to have the unsuspected melanoma fungate out through the nail.

5. *Primary Syphilitic Chancre of Finger.*—The history of exposure (usually in a physician), the location in the nail sulcus, the rapidity of growth, the absence of pigmentation, and the recognition of the *Spirochaeta pallida* on dark-field examination are significant differential points of diagnosis.

6. *Gangrene of the Toe.*—A careful general physical examination always furnishes confirmation of the diagnosis of gangrene of the toes. The patients are usually older than the subjects with subungual melanoma. Coexistent with the gangrene are often such related findings as diabetes mellitus, arteriosclerosis, and hyperpiesia. Gangrene is frequently bilateral and may involve more than one toe. The prodromes of numbness, tingling, and paresthesia and the local picture of the gangrenous lesion are additional diagnostic points in the recognition of gangrene.

7. *Dupuytren's Exostoses* (subungual osteochondromas) of the terminal phalanges are easily recognized on radiographic examination. The greatest difficulty in diagnosis arises in the early tumors in which ossification has not occurred. Lateral roentgenograms reveal the tumor which otherwise may be hidden. It cannot be palpated because of protection by the overlying nail. The true nature of the tumor may be obscured by the common coexistence of marked subungual hyperkeratosis, which seems sufficient on casual inspection to account for the distortion of the nail. (Fig. 5.)

8. *Subungual Fibroma.*—This benign nonpigmented inactive lesion is readily recognized but occasionally required a biopsy for confirmation of the diagnosis. It may be a neurofibroma in some cases; in other instances it is a foreign body reaction about an imprisoned thorn or splinter.

9. *Subungual Keratosis.*—Due to trauma, irritation by a foreign body, or recurrent ringworm infection, the nail may become elevated

and distorted by hyperkeratosis occurring beneath the nail or in the sulcus. Occasionally it is pigmented. It may be precancerous.

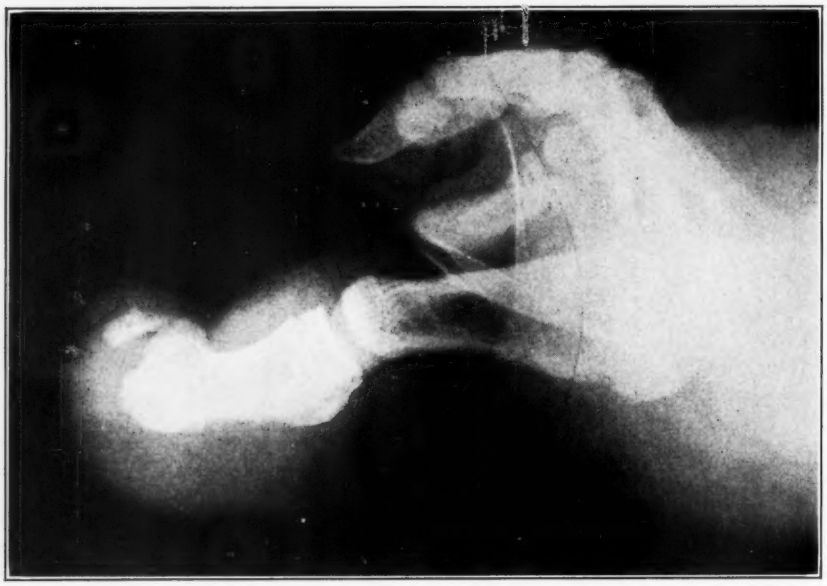


Fig. 5.—Dupuytren's cartilaginous exostosis of terminal phalanx (subungual).

Fig. 6.—Subungual keratosis simulating melanoma.

CASE REPORT.—Mrs. B. B., aged 40 years. In October, 1935, the patient discovered a small black spot under the medial side of the right great toenail. There were occasional pain and some discharge simulating infection. Arising from the matrix

of the toe was a sessile, elevated nodule, measuring 1 cm. in diameter (Fig. 6). It was bluish in color and had some of the clinical features of subungual melanoma. A biopsy was taken; the diagnosis was keratosis. Treatment consisted of a square radon plaque applied for 800 mc. hours at 1 cm. distance, and a radon bulb applied for 500 mc. minutes. Later the nail bed of the great toe was excised. There has been no recurrence.

10. *Subungual Epithelioma.*—With this tumor the nail sulcus rather than the matrix is involved. The epithelioma grows more slowly, ulcerates more quickly, and bleeds less easily than the melanoma of the same location. It differs from the melanoma in being firmer, nonpigmented, and frequently papillary in structure. The epithelioma may be one of many epitheliomas of the skin in the same subject and is frequently associated with such diseases as Bowen's precancerous keratodermas and Darier's carcinosis cutis multiformis verrucosis. Biopsy may be necessary at times in order to plan the method of treatment, as epithelioma usually responds well to radium therapy, whereas melanomas are notoriously radioresistant. We have seen this cancer develop beneath the nails of radiologists afflicted with chronic radiation dermatitis.

11. *Subungual Angiosarcoma (Kaposi's disease).*—This rare tumor is of comparatively slow growth, red and vascular, nonpigmented, and soft. The tumor cells are arranged about the blood vessels in such a manner as to suggest a peritheliomatous origin. Although melanoma metastatic to lymph nodes may resemble primary angiosarcoma of the lymph nodes in histologic appearance, the primary melanomas and angiosarcomas of the nail bed are more obviously distinct clinical and pathologic entities. Kaposi's sarcoma occurs usually on the lower extremities of males, generally those of Slavic, Jewish, or Southern European origin. The tumors are multicentric in origin, so that more than one primary site may exist. They may occur bilaterally. These patients usually have short, thick legs with associated varicosities and occasionally edema of ankles and feet. Other regions on the hands and feet, in addition to the nail bed, are involved. The first lesion is a macule, which under the microscope appears to consist of ectasia of blood vessels and perivascular lymphocytic infiltration. The second stage is an elevated nodular granuloma which does not seem neoplastic. Finally the nodules become confluent and firmer; under the microscope the tumor has protean characteristics, varying in the quantity of angiomatous, myomatous, and neuromatous elements, so that it may resemble a peculiar angioma, or angiosarcoma, endothelioma, fibroma, fibrosarcoma, leiomyoma, etc. The tumor originates probably from the region of the complex neurovascular annexes. Treatment is usually by radiation therapy.

CASE REPORT.—Dr. J. M., aged 54 years. Ten weeks previous to diagnosis he noticed a small ulcer near the lateral sulcus of the nail bed of the middle toe of the right foot. This gradually increased in size and recently had bled. It had not been

painful. There was no history of injury (Fig. 7). A biopsy was taken; the diagnosis was Kaposi's sarcoma. Square radium plaque for 800 mc. hours at 1 cm. distance was given on Nov. 14, 1935.

On April 9, 1937, there was a nodule measuring ½ cm. in diameter on the medial aspect of the left great toe, which was elevated and fiery red. This was excised on April 9. On April 14 a square radium plaque was applied to the toe for a dose of 750 mc. hours. No new nodules have occurred to date.

12. *Subungual Tumors of the Glomus.*—In 1924 Masson described 3 cases of small bluish tumors, subungual in location and exquisitely sensitive. Masson has shown that these tumors arise in organs situated in the field of certain arteriovenous anastomoses and demonstrated nerve

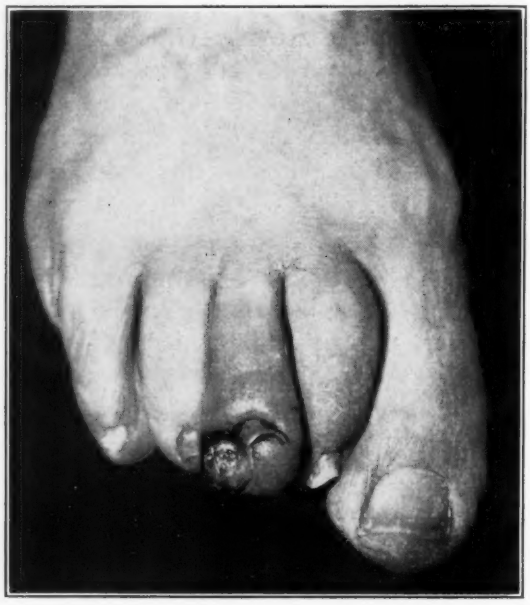


Fig. 7.—Kaposi's hemorrhagic sarcoma developing in nail sulcus.

fibers surrounding the vessels of the tumor, applying to the organ the term "glomus neuromyoarterial." Histologically, the epitheloid cells of Masson surround the arterioles of the glomus, where they intermingle with smooth muscle cells. This vascular neuromuscular organization (glomus) is normally pulsating and aids in regulating the blood pressure to the extremities. The glomus tumors develop most frequently in the nail bed and about the fingers and toes, where the glomus occurs with greatest frequency. In 1936 Geschickter analyzed the 78 verified cases in the literature of tumors of the glomus and found that 22 of the 31 on the fingers were subungual. This is the only tumor in this group which may cause some difficulty in the diagnosis of subungual melanoma. A positive diagnosis can be made only with the microscope. The benign nature, slow growth, absence of metastasis, and

exquisite sensitivity of glomus tumors are important diagnostic criteria. They give rise to sharp, radiating pain, spontaneous in occurrence.

CASE REPORT.—D. H., a physician, aged 48 years. In the posterior portion of the nail of the index finger of the left hand was a rounded tumor lying beneath the nail and measuring about 6 mm. in diameter. It was elevated but slightly, causing a change in the nail bed and the nail from that point forward to the tip of the nail. It was extremely tender to touch. It was deep rose in color. It was a typical glomus tumor, small when first noticed. The patient had scraped and split the nail, relieving the pressure.

Radiation therapy was given first at the patient's request. Five months later the nail was split and in bad condition due to radiation. The patient did not come to a decision as to whether or not the nail was to be removed.

13. *Metastatic Tumors of the Nail Bed.*—This occurrence is so rare as to constitute a curiosity. There have been only 2 such instances in our experience.

CASE REPORT.—M. G., a woman aged 41 years, gave the following history: In 1928, shortly after confinement, she noticed a small lump back of her right ear. This gave no trouble until 1933 when it began to grow. On March 17, 1934, she consulted her physician when the tumor was 4 cm. in diameter. The mass was removed by him on April 2 and proved to be closely adherent to both skin and fascia. The facial nerve was involved and so was sacrificed. The diagnosis was adenocarcinoma of the parotid. On April 13 she was referred for postoperative radiation treatment: radium element pack 24,000 mg. hours at 6 cm. distance, followed by the insertion of gold radon seeds on Oct. 16. On Sept. 20, 1935, there was no evidence of recurrence.

In August, 1935, she crushed the middle finger of her right hand, but noticed nothing unusual at the time other than local pain and discomfort. About Dec. 20 she observed that the finger was becoming tender, swollen, and reddened, with infection in the nail bed. She applied for treatment Feb. 20, 1936.

The infection involved the lateral sulcus and discharged considerable pus. Roentgenograms were made, with a provisional diagnosis of osteomyelitis of the terminal phalanx. On the suspicion that it might be due to metastasis, the lateral third of the nail bed was excised down to the nail sulcus, and immediate frozen section confirmed the diagnosis of carcinoma. An amputation of the distal phalanx was performed, using a ventral flap. On April 3, 1936, the finger was almost healed and there was no evidence of a recurrence of the parotid tumor.

On June 5, 1936, there was a subcutaneous nodule 1 cm. in diameter situated in the side of the finger which was amputated. There was a very large freely movable lymph node in the right axilla.

On June 6, 1937, a left thoracentesis was performed. Death occurred on Oct. 20, 1937. The diagnosis was adenocarcinoma of the right parotid gland with generalized metastases.

THE PROGNOSIS OF SUBUNGUAL MELANOMA

The prognosis of patients with subungual melanomas depends on the presence or absence of metastases to the regional lymph nodes. Melanomas of the nail bed are seen early by the patient because of their conspicuous location, but they are diagnosed by the physician at a late stage in their course because of their confusing resemblance to other

lesions in the region of the nails. Fourteen of the sixteen patients studied at the Memorial Hospital had curettements of the nail beds in other clinics prior to the determination of the correct diagnosis. Incision and curettage of these so-called black cancers are hazardous procedures because they facilitate infection of the tumor and probably hasten the dissemination of the melanoma by metastasis to other regions.

The percentage of cures for subungual melanomas is higher than for melanomas of any other location. The reason for this advantage is not only the slow rate of growth and the late period of dissemination of these tumors, but also the unique location at the terminal ends of the phalanges. This situation is such that amputation of the involved region is usually a curative procedure if no metastases have occurred. Melanomas of other locations are not so amenable to radical surgical extirpation unless crippling deformities or extensive loss of tissue are suffered. The end results are summarized in Table II.

TABLE II

END RESULTS OF SUBUNGUAL MELANOMAS TREATED AT THE MEMORIAL HOSPITAL, 1917 TO 1937, INCLUSIVE

PREVIOUS TREATMENT AND CONDITION AT TIME OF ADMISSION TO MEMORIAL HOSPITAL	TOTAL	DEAD	ALIVE*	
		WITH RECURRENCE	WITH NO EVIDENCE OF RECURRENCE	WITH RECURRENCE
Total	16	8	5	3
1. Amputation elsewhere, with involvement of nodes on admission	7	6 mo. (5 cases)	15½ yr.	2¾ yr.
2. Curettement elsewhere with involvement of nodes on admission	3	4 mo. 1 yr.	8 yr and 7 mo.	
3. Curettement elsewhere, with no involvement of nodes on admission	4		5 mo. (under treatment) 2½ yr. 9¾ yr.	5¼ yr.
4. No previous treatment, except salves, with no involvement of nodes on admission	2	3¼ yr. (immediate recurrence)	2 yr.	

*Five-year survival: Alive, with recurrence, 1 (6.25 per cent); alive, with no evidence, 3 (18.75 per cent)=4 (25 per cent).

TREATMENT

All reported cases of subungual melanoma have been treated by surgical intervention. Malignant melanomas of all locations are notoriously radioresistant and those located in the nail bed are doubly so because of their situation. The nail bed is not a good tissue for the reaction which accompanies curative doses of radiation. The dose of radium or roentgen rays necessary to sterilize a subungual melanoma must be almost caustic in effect. If primary healing of the radiation

reaction occurs, it is often followed by late radionecrosis and a painful useless finger tip or toe. Preoperative irradiation is no longer employed for melanomas of this particular location.

Necessity for Early Amputation.—Once the diagnosis of subungual melanoma is made, amputation of the digit should be considered as an emergency, because the day or time of the metastases can never be foretold. The number of phalangeal joints to be sacrificed depends on the proximal extent of the tumor. Conservative surgical excision with preservation of the terminal phalanx is hazardous.

Fig. 8.—Recurrent myxomatous cyst of nail bed and nail matrix.

Prophylactic Dissection of Regional Nodes.—A study made two years ago of all malignant melanomas of the extremities revealed the distressing information that radical dissection of the primary melanoma often was not curative in itself, even in patients in whom no regional lymph nodes were palpable. Some of these patients would return during their observational period with large confluent nodes containing metastatic melanoma which was not observed at the previous visit. The decision was made to dissect out the regional lymph nodes as a routine procedure even if the nodes were not palpable. The wisdom of this routine practice has been proved by the subsequent micro-

scopic studies of these lymph nodes removed prophylactically; in two-thirds of the cases minute foci of metastatic melanoma (clinically undetectable) were found (Case 14). Therefore, the dissection of lymph nodes is performed in all patients, whether the lymph nodes are enlarged or not.

Interval Between Amputation and Regional Lymph Node Dissection.—Another observation has been that an element of danger exists in performing both the excision of the primary melanoma and the dissection of regional lymph nodes at the same operative séance. This procedure

Fig. 9.—Recurrent melanoma of arm, thumb, and axilla.

has been followed too frequently by the development of new melanotic nodules in the intervening limb or by diffuse recurrence in the axillary or inguinal wounds (Fig. 9). The practice now is to amputate first, then perform the regional lymph node dissection one to two weeks later if there is gross evidence of metastatic involvement and six weeks later if the dissection is considered prophylactic. If melanoma cells are in transit in the lymphatics, they may be filtered out in the lymph nodes during this time; whereas, in the previously stated

method of surgical treatment, they may grow in blocked lymph vessels or be emptied into a fresh wound.

The following case reports represent the different groups included in Table II:

1. *Amputation Elsewhere With Involvement of Regional Nodes at the Time of Admission to the Memorial Hospital.—*

CASE 1.—M. V. T., a woman 40 years of age, applied to the Memorial Hospital Nov. 7, 1933.

Four years before the patient had had a slight injury to her left index fingernail. She thought a splinter was lodged therein. There followed a long series of treatments for paronychial infection. About twelve curettements of the nail bed were done for more than three years. The terminal phalanx finally was amputated. Six months later the terminal portion of the amputated finger became enlarged, red, and extremely painful. Following this a second amputation was done so that the second phalanx was removed. Within a few more months the proximal phalanx was removed.

During the last year the patient noted the continuous appearance of new subcutaneous nodules in the palm, forearm and arm, left chest wall, left abdominal wall, scalp, and left back. Some of these nodules have been excised and others treated by the insertion of gold seeds. The regression of the nodules treated by radiation indicated that the tumor had at one time been rather radiosensitive.

In the scalp there were from six to eight subcutaneous nodules varying from 4 to 8 mm. in size. In the left palm and in the subcutaneous tissues of the left forearm and arm there were about twenty subcutaneous nodules, the largest of which was 2 cm. in diameter. The abdomen showed no enlargement of the liver or palpable masses. A diagnosis was made of malignant melanoma with dissemination.

Palliative doses of roentgen rays and radium were given to all the known melanotic nodules during the next three months. There was no appreciable local or constitutional benefit.

Her condition was unimproved. The patient died on Nov. 7, 1933.

CASE 2.—R. B., a male aged 53 years, applied to the Memorial Hospital Sept. 14, 1931.

In 1925 a sore appeared under the nail of the great toe of the right foot. The nail crumbled. Iodine was applied, which desiccated the sore. The nail grew out again and a discharge appeared. The nail was removed and the nail bed scraped. When the nail grew out again, the discharge recurred. From 1926 to 1928 there were several curettements. In 1930 x-ray treatments were given, with no response. In January, 1931, there was evidence of metastasis to the right groin. In April, 1931, the matrix of the diseased nail was cut away. In June, 1931, there was swelling of the left cervical lymph nodes. In August, 1931, a roentgenogram of the chest revealed pleural metastasis. The patient coughed up black clotted blood.

On admission the right toe had been amputated through the distal joint, with no recurrence in the stump. Dotted over the patient's trunk, arms, and thighs were numerous subcutaneous, firm nodules, spherical and oval, varying from 0.5 to 3 cm. in diameter. Some of the smaller nodules were surrounded by zones of ecchymosis. In the right groin was a group of enlarged elastic nodes and in the left supraclavicular space was a mass 5 cm. in diameter over which the skin was reddened.

Certain facts in this case, such as the widespread rapid dissemination, the occurrence of ecchymosis accompanying the appearance of new nodules, the fact that the patient had noticed spontaneous regression of some nodules and that he noted some regression of the tumor in the right groin following x-ray treatment, all suggested that this melanoma might be somewhat more radiosensitive than usual.

He was admitted to the ward for continuous irradiation to the entire body by the Heublein unit, Sept. 15 to Oct. 12, 1931, 523 hours, 225 r. On Nov. 3 new metastatic melanomas appeared, and the patient gradually became worse. At his own request, on Nov. 14, the patient was transferred to a hospital in Connecticut where he died on Dec. 9.

The autopsy report showed the following organs involved: sternum; pleural surface of the pericardium over the right auricular region; heart, just under the endocardium, in the right auricle a small tumor; lungs; abdomen, chiefly in the mesentery of both large and small intestines; extensive involvement of the retroperitoneal lymph nodes, the urinary bladder, and kidney.

CASE 3.—E. W., a negro male laborer, aged 59 years, applied to the Memorial Hospital on Aug. 2, 1928. He had always been in good health until the present illness.

Early in 1926 he injured his left thumbnail. After some palliative treatment, the nail was removed, but the lesion grew rapidly to involve the entire distal phalanx. At another hospital in December, 1927, an amputation was performed at the metacarpophalangeal joint. The wound healed satisfactorily by primary intention. In May, 1928, the patient felt a small mass in the left axilla, which grew rapidly.

On examination at the Memorial Hospital, the wound at the base of the left thumb appeared to be healed with no evidence of disease. In the left axilla there was a hard, fixed, inoperable mass composed of fused nodules the size of an orange. The mass extended anteriorly and subpectorally. There was free arm motion. Another node was felt in the supraclavicular region. A radiograph of the chest was negative for metastasis.

Microscopic examination of the tumor of the thumb showed a melanoma composed of interlacing fusiform cells with hyperchromatic nuclei and abundant intra- and extracellular pigment. There were frequent mitoses. The cells were arranged in infiltrating strands and whorls, characteristic of melanosarcoma. The diagnosis of melanoma was confirmed by Dr. Ewing.

The left axilla and left supraclavicular space were treated by combined external irradiation, using high voltage x-rays and the radium element pack.

On Oct. 24, 1928, the axillary and supraclavicular nodes appeared slightly smaller. On Nov. 28, 1928, the axillary tumor showed definite diminution in size, but both supraclavicular fossae contained hard palpable nodes. On Jan. 1, 1929, information was received of the patient's death. In the terminal period of his disease he suffered severe pain in his head, particularly at the base of his skull. No necropsy was performed.

CASE 4.—C. D., an Irish woman, 46 years old, applied to the Memorial Hospital on March 13, 1934.

A window sash had fallen on her finger about a year previously, and for about a month afterward the finger was black and blue, quite painful, and swollen. This disappeared, but a few weeks later there was a blackish blue discoloration of the nail bed extending into the skin around the base of the nail. There was occasional bleeding but never any formation of a demonstrable tumor or an ulcerated lesion. In October, 1933, amputation was performed, at the interphalangeal joint, followed by an uneventful convalescence.

The patient's general health had been excellent until about two weeks prior to admission to the Memorial Hospital, when she noticed shooting pains under the right armpit, and about ten days later there was a hemorrhagic discoloration of the skin of the right breast. She noticed the coincidental presence of a mass in the right axilla. She was referred from another hospital for further treatment.

Examination showed no evidence of recurrence in the right index finger. In the right axilla was a bulky indurated movable mass measuring about 6 by 8 cm. in diameter. The skin of the tail of the right breast was yellow and erythematous in blotchy areas. A film of the chest showed a small circular shadow of increased density measuring about 1 cm. in diameter in the lateral portion of the right subapical region, with another nodule, somewhat larger in size, just lateral to the lower pole of the left hilus region. These nodules represent metastases.

On March 14, 1934, a palliative left radical mastectomy was performed. Convalescence was uneventful.

On May 5, 1934, the patient was admitted to the observation ward at the Bellevue Hospital. From there she was transferred to the Manhattan State Hospital where she died on June 15, 1934. The diagnosis was psychosis with cerebral arteriosclerosis.

CASE 5.—G. S., a machinist, aged 62 years, applied to the Memorial Hospital on Oct. 10, 1934.

In March, 1933, the patient hit his thumb with a hammer. The blow knocked off part of the side of the thumb, leaving a raw bleeding area at one side of the nail. The lesion never healed, but slowly increased in size, forming a cauliflower tumor which bled easily and was dark in color. In August, 1933, the thumb was amputated. At this time a tumor developed in the left forearm and a tumor in the left axilla was noted. A month later axillary dissection was done. The patient was free of symptoms for several months. Then the tumor recurred under his arm, growing steadily, and the tumor on the forearm increased in size.

Examination revealed the left thumb missing beyond the interphalangeal joint. On the skin of the forearm about midway between the wrist and the elbow over the radius was a tumor 2 cm. in diameter. The tumor in the left axilla measured 18 by 13 by 22 cm.

X-ray treatment in fractionated doses was given from Oct. 11 to Oct. 25, 1934, to the left shoulder girdle, anterior, posterior, and lateral fields.

The general condition of the patient was not good enough to permit an interscapulothoracic amputation.

On Jan. 7, 1935, the patient complained of pain in the small of the back, suggesting involvement of the lumbar vertebrae. There was a bulky axillary and left supraclavicular involvement and many skin nodules on the left chest wall as well as the upper arm. The liver was greatly enlarged, and the patient was considered to be in the terminal stage. He died on Jan. 26, 1935.

CASE 6.—F. W., a physician, aged 71 years, applied to the Memorial Hospital, March 18, 1935.

In 1887 an ingrown nail on the right big toe was removed but the matrix continued to grow. This overgrowth of the matrix was removed in 1933. The nail did not grow and an ulceration appeared over the nail bed. This bled easily and an offensive discharge was constantly present. During the course of a year, he received two x-ray treatments and one radium pack treatment. The lesion healed temporarily. In 1934 the first toe was removed with resection of the inguinal lymph nodes. The patient then went to England where he had resection of the femoral lymph nodes and x-ray therapy over the iliac region, two ports, anterior and

posterior over the right lower quadrant. A week prior to admission a small node was removed from the scar over the femoral region. The report was positive for melanoma.

The physical examination revealed an elderly man in excellent condition for his age. The area over the right inguinal region and over the right femoral region showed operative scars and radiation effects, induration and thickening of the tissues. There were a few soft palpable nodes in the left inguinal region.

The treatment at the Memorial Hospital consisted of external irradiation using fractionated doses of high voltage x-rays and a similar plan of radium pack exposure. Two series of treatments by Coley's toxins were given intramuscularly and intravenously for a total of twenty-five injections.

A second femoral dissection was advised, but the patient decided to return to Toronto, where this operation was performed on June 24, 1935.

CASE 7.—C. A., a white male clerk, aged 30 years, applied to the Memorial Hospital on Aug. 4, 1922.

About four and one-half years prior to application, the patient observed a small black streak in the right thumb nail, which persisted and gradually increased in size to involve the entire nail. The nail finally became ulcerated. The nail was curetted but did not heal, and the lesion increased in size. Another curettage was done without improvement. In April, 1922, four months before application, the patient noticed a lump about the size of a small egg in the right axilla. This axillary tumor and the two distal phalanges of the involved thumb were removed at another institution in July, 1922. Microscopic preparations of these tumors were loaned to the Memorial Hospital, where the diagnosis of malignant melanoma was made.

On admission a small skin nodule was found near the scar of the thumb. A thickened plaque 2 by 3 cm. in diameter was present in the lower end of the linear axillary scar. A node of suspicious character could be felt high in the right axilla. It was difficult clinically to determine whether this induration and lymphadenopathy were recurrent melanotic tumors or inflammatory swellings.

The nodules on the thumb and in the axillary scar were treated by low voltage roentgen rays and by the application of small radium plaques at a distance of 1 cm.

The nodule on the thumb and the indurated plaque in the axillary scar had disappeared completely by Aug. 12, 1922, which is sufficient evidence to question the neoplastic nature of these so-called recurrences. There was no evidence of disease at the last examination on Aug. 1, 1935.

2. *Curettement Elsewhere, With Involvement of Regional Nodes at the Time of Admission to the Memorial Hospital.*—

CASE 8.—J. D., a clothes operator, aged 64 years, applied to the Memorial Hospital on June 6, 1934.

Six years prior to admission, he had pinched his left thumb in a machine, following which a black discoloration appeared under the nail and the nail came off. About three years before admission, he noticed a small granular outgrowth on the dorsal aspect of the nail bed. A biopsy was done at another hospital, with the diagnosis of "infiltrating nevocarcinoma of the melanoma type." Nine days later he received two skin units of x-ray therapy. The wound healed and the patient had no further trouble until April, 1934, when he pricked his thumb with a needle. A small granular nodule appeared which gradually increased in size. About this time he noticed a mass in the left axilla which gradually increased in size. He was referred by the hospital which had made the previous diagnosis.

The examination revealed the nail absent from the left thumb, an atrophic appearance of the entire thumb, the skin smooth and epilated. The nail bed had a granular appearance and in the center of it was a rounded firm granular tumor

Fig. 10.—Subungual melanomas. *A*, Case 8; *B*, Case 11; *C*, Case 13; *D*, Case 14; *E*, Case 15; *F*, Case 16.

measuring about 8 mm. in diameter (Fig. 10*A*). In the left axilla there was a large, firm, movable lymph node about the size of a lemon.

On July 7 the left thumb was amputated and a left axillary dissection was carried out. The microscopic examination of the specimen from the thumb amputated

at the metacarpophalangeal joint showed melanoma, grade III. The microscopic examination of the axillary lymph node showed melanoma, grade III.

Both wounds healed by primary intention, and the patient was discharged in good condition on July 18, 1934. When he reported on Sept. 17 there was no evidence of disease but considerable lymphedema of the left arm. The arm could not be extended above the level of the shoulder.

On Oct. 10 the patient's physician telephoned that he was hemiplegic (a sudden vascular accident) and that his condition was critical. Word was later received of his death on that date.

CASE 9.—A. T., a man, 59 years of age, applied to the Memorial Hospital on April 15, 1930.

Three years prior to admission a chiropodist cut the nail of the great toe. This did not heal and so-called "proud flesh" had grown over the edge. He was operated upon in Germany and a skin graft was done.

On admission the end of the great toe was occupied by a tumor about 3 cm. in diameter. It bled fairly easily but was not tender. In the left inguinal region were a few rather firm nodes and a few other firm nodes running along the course of the femoral vein.

On April 16, 1930, the patient was admitted for amputation of the left great toe and excision of the tumor in the left groin. The inguinal nodes and surrounding fat were removed en masse. One node about 2 by 2 cm. in size was seen to contain metastatic melanoma. The pathologic report showed the contents of the inguinal region to be fat and fibrous tissue, at one end of which were two inguinal nodes, intensely black, fairly soft, and evidently containing metastatic melanoma.

The great toe was amputated. The pathologic report was as follows: The nail is absent. Springing from the matrix of the nail is a fungating tumor with overhanging everted margins. It is roughly divided into three distinct lobulations. The margin of the toe is surrounded by a thin border of black which is characteristic of subungual melanoma. The tumor proper is reddish gray, with one small central pigmented spot. On the medial side of the toe, 5 cm. posterior to the line of excision, is a tiny black spot firmly attached to the fascia.

On May 29, 1930, the patient was discharged in good condition. When seen in the clinic on Oct. 15 there was no evidence of disease. Death occurred in May, 1931.

CASE 10.—W. M., a white male, aged 34 years, applied to the Memorial Hospital on May 27, 1929.

Two years previously a small black spot had appeared on the nail of the right forefinger. This gradually increased until the whole nail was black. There was no pain nor any similar change in any other part of the body. His physician discovered an enlarged lymph node in the infraclavicular region and a nodule in the right chest. These were not typical of melanoma, but external radium therapy was given, with disappearance of the questionable lymph node and cutaneous nodule.

On May 15, 1930, as the disease seemed to be getting worse, amputation was advised. This was refused. The patient then went to Germany where scrapings from the blackened nail were examined microscopically and found on culture as well to contain a black pigment-producing fungus (onychomycosis nigrescens). On his return to the United States, bearing these cultures with him, he ridiculed the original diagnosis of subungual melanoma. The diagnosis was adhered to, however, because of the coal black line of pigment bordering the nail. Finally, he consented to amputation, and the specimen was then found to be true malignant melanoma (Fig. 4). On a clinic visit on Feb. 20, 1933, there was no evidence of disease. On June 14, 1935, the patient wrote that he was feeling well and was having no further trouble.

3. *Curettement Elsewhere, With No Involvement of Regional Nodes at the Time of Admission to the Memorial Hospital.—*

CASE 11.—C. R., a male, aged 64 years, applied to the Memorial Hospital on May 28, 1935.

About ten years before this, the patient had noticed a black band involving the central subungual tissues of the right index finger. This remained static for seven or eight years, then disappeared completely. Sometime later a similar discoloration appeared at the mesial edge of the nail, involving the tip of the finger. In January, 1935, a small pigmented papillary tumor developed at the mesial edge of the nail, near the center of the previously described area. This small tumor, the size of a pea, was removed on April 1. Healing was progressive. There was no pain and no evidence of inflammation.

Examination showed that the mesial half of the nail of the right index finger had been removed. The remaining half was somewhat elevated. There was a black pigmentation of the soft tissues of the tip of the finger which extended into the subungual region. (Fig. 10*B*.) There was evidence of rather recent infection. There were no palpable lymph nodes in the right axilla.

On June 3 the finger was amputated at the level of the midphalangeal joint. Later, additional incision and drainage were done in order to lessen the severity of the hand infection. On July 3 the patient was discharged, to return twice a week for dressings. On Sept. 23 the hand was well healed, with excellent function. There were no palpable right axillary lymph nodes. In view of the patient's age and recent hospitalization, prophylactic axillary dissection was not done. The patient has been alive with no evidence of recurrence for two and one-half years.

CASE 12.—C. M., a physician, aged 46 years, came to the Memorial Hospital in January, 1932. At that time he was under the care of a Boston surgeon who wished an opinion. Dr. Ewing termed the biopsy an extremely low-grade but definite subungual melanoma. Amputation of the terminal phalanx was advised, but it was not done in Boston.

In 1924 the patient had noticed some discoloration of the nail which looked like a sliver. The nail was intact for about a year, then started to discharge, becoming a chronic whitlow with attacks of acute inflammation. In March, 1931, he injured his left thumb, following which some of the nail was removed. There was a second injury in June, 1932. The nail had been removed on three different occasions.

On Sept. 13, 1932, he made application to the Memorial Hospital. The examination showed a perfectly definite black recurrence in the nail bed, measuring roughly 3 by 5 mm. There was also one tiny suggestive nodule lateral to this but it was too small to be certain whether this was a recurrence. There was an enlarged node in the left midaxilla. He complained of some pains in the lower lumbar region. His general health was good.

On Sept. 13, the terminal phalanx of the left thumb was amputated. The microscopic report gave the diagnosis of melanoma. Aspiration biopsy of the axilla showed no tumor cells.

The left axilla received 58,000 mg. hours of radiation by a 4 gm. radium element pack applied at a radium skin distance of 10 cm.

In October, 1932, the nodes in the axilla were much smaller, and a year later they had disappeared and there was no evidence of disease. In November, 1934, they recurred, and a month later the patient wrote for advice regarding the axillary dissection. In January, 1935, this was done in Boston. In June, 1935, the chest was completely filled with metastatic nodules. The liver was not enlarged, and there was no evidence of metastasis other than in the chest. The date of death was not ascertained.

CASE 13.—M. P., a Russian Jewish housewife, aged 57 years, applied to the Memorial Hospital on April 4, 1928.

In 1926, two years prior to application, the patient noticed bleeding under the right great toenail. The nail was split but not elevated. No pain was experienced at this time. The bleeding continued until the nail was partially removed and the lesion curetted at another hospital in September, 1927. On Nov. 28, 1928, the sanguineous discharge recommenced. Sudden severe pain was felt in the toe on March 16, 1928.

Under the right great toenail was an ulcerated, reddish tumor measuring 2 by 1 cm. and elevating the nail (Fig. 10*C*). There were no palpable nodes in the popliteal or inguinal regions. A biopsy was reported on March 13, 1928, as suggestive of melanoma.

On March 25, 1928, the great right toe was amputated at the midpoint of the first metatarsal bone. Section through the toe and lesion showed numerous granular areas, flecked with brown pigment. The microscopic diagnosis by Dr. Ewing was melanoma, grade III, radioresistant. Histologically the tumor was composed of solid sheets of cells with very few invasive tendencies. The overlying epidermis was thin and flattened by the pressure of the subjacent tumor. There was considerable lymphocytic infiltration of the stroma. The cells were large, spheroidal, and epithelioid, with granular cytoplasm, large ovoid nuclei, and well-marked nucleoli. There were very few spindle cells and infrequent areas of pigmentation.

On May 1, 1929, one large lymph node of indefinite nature was felt in the right inguinal region. An immediate treatment was given by the radium element pack. The node disappeared and there has been no further evidence in the foot or in the groin, a survival of nine and three-fourths years.

CASE 14.—A. R., a woman, 50 years of age, applied to the Memorial Hospital on July 21, 1937.

In August, 1936, the patient had scratched her finger with a piece of tin. This healed, but three or four months later she hit the same region on a gas jet. A granular structure came on the dorsum of the right forefinger just beneath the level of the nail. It was incised several times and then disappeared. It recurred about three months prior to application. It drained some pus and grew so rapidly that it involved almost the entire distal portion of the terminal phalanx of her forefinger.

The examination showed a soft, lobulated, radiating tumor of the nail bed, pushing the nail upward and forward and splitting it and extending to the distal phalangeal joint (Fig. 10*D*). It was smooth and apparently not ulcerated. It had many features of a pyogenic granuloma. The biopsy was reported as malignant melanoma. The lymphoid tissue in the right axilla could be palpated, but there were no discrete nodes discernible.

On Aug. 6, 1937, the right index finger was amputated at the second phalangeal joint. The wound healed satisfactorily. On Sept. 15, 1937, a right axillary dissection was performed. In the section of the fat three nodes were found, the largest of which measured 2.5 cm. in diameter. The microscopic examination showed melanoma in the peripheral sinus of one of the nodes.

On Oct. 11, 1937, the finger was well healed, and there was no evidence of disease. At the end of 1937 the patient was still reporting to the clinic.

4. *No Previous Surgical Treatment.*—

CASE 15.—K. T., an Irish woman, aged 57 years, applied to the Memorial Hospital on June 8, 1927.

Ten years previously, in 1917, this patient had injured the fourth toe of her left foot. Soon afterward she noticed a patch of bluish discoloration, 0.5 cm. in diameter, in the region of the nail sulcus. She insisted that prior to the injury the toe had

been perfectly normal. The bluish discoloration persisted without change in size or color until January, 1927, when it began to grow and soon became ulcerated without obvious cause. The only treatment had been the application of sundry salves to the toe.

On the outer surface of the left fourth toe, there was an elevated, ulcerated tumor, 3 by 2 by 2 cm. (Fig. 10*E*). This mass was soft and slightly movable on the toe. A radiograph of the foot on Aug. 16, 1927, showed atrophy of disuse, but no evidence of invasion of the bones of the foot by the tumor.

While the patient was awaiting admission to the hospital, she received one high voltage roentgen-ray treatment over the involved toe. On June 29, 1927, the fourth toe was amputated. The histologic diagnosis of the tumor by Dr. Ewing was nonpigmented melanoma, grade III. The wound healed satisfactorily. On Aug. 9, 1927, a small brown lump was noted in the center of the scar of amputation. This nodule was excised on Aug. 18, 1927. Histologic examination of this tissue showed a few pigment-bearing cells in the vessel sheaths of the derma but no definite tumor tissue. The patient was seen periodically in the clinic until April 4, 1928, during which time there was no evidence of recurrence. She was lost to observation until Nov. 5, 1928, at which time the toe stump was well healed, the general health good, but a large hard tumor was evident on the inner aspect of the left thigh.

The patient refused surgical and radiation treatment. Several new tumors appeared on the left leg. In June, 1929, these tumors were excised at another hospital. In August, 1929, the lower end of the recent incision was hard and slightly elevated by a recurrent tumor mass. In September, 1929, the scar on the thigh was surrounded by many hard subcutaneous nodules. In November, 1929, she complained of severe pain in the lumbar region. New tumor masses were evident in the left groin and popliteal space. In December, 1929, the tumors on the thigh were increasing in size and many new nodules had appeared over the entire leg. There was rapid loss of weight and strength. On Jan. 22, 1930, when last seen, the patient was bedfast and seemed to be completely paralyzed. This condition was attributed to cerebral metastases. Death occurred on Sept. 7, 1930.

CASE 16.—M. G., a white woman, 68 years of age, applied to the Memorial Hospital on Nov. 18, 1935.

About five years previously the patient had noticed a small black area on the skin bordering the nail bed of the left great toe. This became infected and she was treated at another hospital four and one-half years ago with ointments, whirlpool baths, and lamps. The nail became markedly deformed at that time. She then went to a dermatologist who prescribed an ointment, diagnosing the disease as probable ringworm. The condition improved until about three years prior to application. She noticed that the skin on the dorsum of the toe was gradually becoming black. Two years before application she noticed a black area on the anterior and ventral surfaces of this toe, which had slightly increased in size. Five weeks prior to application she went to the clinic of another hospital. Amputation was advised, but she refused to have it done. This hospital referred her to the Memorial Hospital.

On examination, in the dorsum of the left great toe there was a black area measuring in its largest diameter 2.5 by 2.5 cm., irregular in outline, with sharply defined borders. The nail was deformed and thin in its anterior portion. In the anteroventral surface of the great toe there was one black area 1.5 cm. and discoloration of the skin, with moderate keratinization of the central area (Fig. 10*F*). Situated in the dorsum of the second toe there was a small 2 mm. darkened area, in the web directly between the second and third toes another one, and in the medial ventral aspect of the arch two other small 2 mm. pigmented areas. There was no inguinal adenopathy.

Amputation was advised and the condition explained to the patient's daughter The patient refused to consider amputation. However, later she consented and amputation was done in May, 1936. There is no evidence of recurrence either locally or in the groin. The liver is still slightly enlarged. The patient is still being followed.

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ANGIOMATOUS TUMORS OF THE HANDS AND FEET

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THE term angioma is here used to include all those tumors arising from blood and lymphatic vessels and the various components which go to make up these structures. While angiomatous tumors are not strictly limited to the extremities, certain members of this group, such as the angiomyoneuromas, are rarely found elsewhere, and in Kaposi's hemorrhagic skin sarcoma the initial lesion is most frequently found on the extremities.

The nomenclature of angiomatous tumors is confusing, and in the past there has existed considerable difference of opinion as to the method of classification of these tumors. In the older literature a confusion of terms has grown up, many of which do not represent clinical or pathologic entities. On the other hand, any classification may be unsatisfactory since there is frequent difficulty in reconciling the clinical course of some of these tumors with their histopathology. Some of the obvious clinical features of these tumors may not be manifest in a classification based strictly on histopathology. Such, for instance, are the difficulties encountered in attempting to explain the difference in appearance, rate of growth, character of pain, and metastasis in angiomas presenting very similar microscopic pictures.

I. Angiomas
   a. Vascular malformations
      1. Arteriovenous fistulas
      2. Telangiectasis (port-wine stain, hemangioma simplex, vascular naevi)
      3. Angioma (venous, arterial, lymphatic)
   b. Angioblastomas
      1. Hemangioblastomas
      2. Lymphangioblastomas

II. Angiomyoneuromas (glomus)

III. Kaposi's disease (idiopathic multiple hemorrhagic sarcoma)

The multiple etiologic factors in vascular tumors are again confusing, particularly the tissue of origin. This is illustrated by the difference of opinion among the pathologists as to what should or should

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not be called an endothelioma. The vast majority of vascular tumors are congenital, or at least the anlage is present early in life, even though the tumor may not become manifest until old age. It is frequently difficult, therefore, to determine whether trauma is a primary or secondary factor in the etiology.

Angiomatous tumors may be classed under three main divisions. The first group, the angiomas, is composed of angiomatous malformations and angioblastomas. The angiomatous malformations include a variety of conditions, both congenital and acquired, in which it appears that intravascular pressure and local changes in the vascular wall play a paramount role and in which there is little evidence of true neoplastic tissue. The angioblastomas include those tumors made up chiefly of masses of angioblastic cells undergoing rapid proliferation and which appear to be true neoplasms. Mechanical factors may also play a role in this group in determining the size and progress of the tumor. The second group of angiomyoneuromas is composed of those tumors having a specific histology, as the name implies, and arising from a specific and now well-recognized structure, the glomus. The third group, Kaposi's hemorrhagic skin sarcoma, is included among the vascular tumors with some misgivings, since its etiology is unknown. However, the tumors seem to be composed chiefly of vascular tissue.

Angiomatous tumors, with the exception of Kaposi's hemorrhagic skin sarcoma, are of importance chiefly because of the symptoms they produce, rather than because of danger of malignant change. The question as to whether the term malignant may be applied to angioma has been much discussed. Many of these tumors are locally invasive, eroding through bone, and when vital structures are involved they may result in death. This, however, only rarely occurs in the extremities, and then usually in infants and associated with secondary infection. There has also been much discussion as to whether these tumors take on malignant features from the standpoint of remote metastases. Isolated case reports (Borrmann, Sherman, Ewing, Langhans, Wright) have appeared from time to time in the older literature, the majority of these tumors having occurred in the internal organs. In many of the earlier case reports it seems quite likely that the tumors are not strictly of angiomatous origin. Metastatic tumors of the thyroid and kidney, as well as nonpigmented malignant melanomas and adenocystic basal cell cancers, have been mistaken for angioblastomas. However, there seem to be a few isolated authentic cases of metastasizing angioblastomas occurring on the extremities (Ward and Jonas).

There have been a number of sarcomas reported (Speciale) as arising from the sheaths of blood vessels, several of which have occurred in the extremity. There is also a large group of tumors under the

classification of endothelioma without angiomatous features. Because the histogenesis of these two groups of tumors is still not clearly established, they are not included in this paper.

ANGIOMA

The term angioma includes a variety of vascular alterations, many of which present few if any characteristics which would class them as neoplasms. In the present discussion we have divided the angiomas into two groups: (1) those which may be considered as vascular malformations, and (2) those which may be considered as true neoplasms. The latter we have designated as angioblastomas.

In Geschickter's review of 300 cases of angiomas of the skin including all types, one-third were found in children under 10 years of age and of these 80 per cent were under 5 years. This age distribution fully emphasizes the importance of the congenital origin of many of these tumors. Nearly one-third of the angiomas of the skin appear on the extremities.

Vascular Malformations.—Certain anatomic and physiologic observations have yielded information which is of value in explaining some of the vascular malformations. Sabin has pointed out that the primitive vascular anlage is laid down in solid cords of angioblastic cells. An apparent liquefaction then takes place in which there develop spaces filled with plasma. These later develop into minute vessels or capillaries. The Swiss anatomist Aeby in 1868 expressed the opinion that the vascular system early in its development existed as a uniform capillary network of vessels. This idea was strongly opposed until injection methods finally established the essential truth of the statement. Evans has pointed out that the larger vessels come into existence only by the enlargement of certain fortuitously situated capillaries which assume a larger and larger function and develop into arteries at the expense of other capillaries which accordingly must regress. There are, however, other methods of development by branches from embryonic arteries and in the large organs Mall has demonstrated the development of a vascular system from the so-called sinusoids.

Thoma and other investigators have demonstrated that the size of a vessel and the thickness of its wall are dependent on the rate of flow and the intravascular pressure respectively. He states: "The increase in the size of the lumen of the vessel or what is the same thing, the increase in the surface of the vessel wall, depends on the rate of the blood current. The surface of a vessel wall ceases to grow when the blood current acquires a definite rate. The vessel increases in size when this rate is exceeded, becomes smaller when the blood stream is slowed and disappears when it is finally arrested." "A second histomechanical principle may be added to this, viz., the growth in the thickness of the wall is dependent upon its tension. Further, the

tension of the wall is dependent upon the diameter of the lumen of the vessel and upon the blood pressure." These observations have been elaborated by others by the transplantation of segments of an artery into a vein and vice versa. It has been found that the transplanted segment takes on the characteristics of the vessel into which it has been transplanted. This observation is of importance in consideration of the many arguments as to whether a given angioma has arisen from an artery or a vein. Another, but less well understood, structure which may play an important role in angiomas is the arteriovenous anastomosis, the development of which has been described by Clark and co-workers.

Fig. 1.—Angioma (vascular malformation) composed of numerous endothelial lined spaces in a loose connective tissue stroma without evidence of angioblastic proliferation (×100), hematoxylin and eosin.

The above observations indicate some of the factors at work in the development of the normal vascular system, and unquestionably play an important role in the development of these angiomatous malformations. It is not clear whether a simple vascular malformation may develop later into an angioblastoma, but the evidence would indicate that such a transformation may occur.

Congenital arteriovenous fistulas are formed of fairly well developed arteries and veins, but frequently associated abnormalities of the various layers of the walls of the vessels are found. These are characterized by nodular overgrowth of the intima, imperfect formation of the media with a tendency to form leiomyomatous nodules and aneurysmal outpocketings. While such angiomas may develop rapidly,

forming large tumors, there seem to be no other characteristics suggesting that they are true neoplasms. Obliteration of the arteriovenous opening or thrombosis of the vessels will result in a cure, although the number of intercommunications may be so great as to render this a major surgical procedure, or impossible. Reid, Holman, and others have emphasized the need for early intervention and have pointed out the likelihood of cardiac damage.

Occasionally such arteriovenous communications are seen in their simplest form, as the so-called "spider naevus" appearing on the skin. Pressure with a glass slide will reveal the minute central artery feed-

Fig. 2.—lymphangioma of leg showing site of operative drainage through which an abundance of lymph escaped.

ing the surrounding venules. These frequently disappear spontaneously, presumably by thrombosis, or they may develop into angioma. When seen in their early stages, obliteration of the small central artery by any means will result in a cure. Another group of angiomas is composed of what appear to be veins. They enlarge very slowly, usually in the subcutaneous tissues, presenting a bluish appearance. Occasionally they are painful. The port-wine stain or telangiectasis presents another of these vascular malformations. It is composed of masses of dilated capillaries with no evidences of proliferation.

Malformations of the lymph vessels similar to those seen in blood vessels are described. These lymph vessel malformations appear to be rare on the extremities. The following is an illustrative case report:

CASE 1.—W. Y. (No. 62552), a 14-year-old boy, entered the New Haven Hospital Aug. 7, 1938, complaining of a swelling on the medial aspect of the left thigh of ten years' duration. At the age of 4 years, he had had poliomyelitis and while in the hospital a swelling appeared on the left thigh just above the knee which was mistaken for an abscess and incised, but only clear fluid was obtained. Since that time the tumor had slowly grown larger. The scar had developed a marked keloid and at intervals would break down and a considerable quantity of clear fluid would drain. Physical examination revealed a doughy tumor of indefinite outline, 6 inches in diameter.

The overlying skin had the appearance of an ill-defined port-wine stain on which there was an increased hair growth. At operation the tumor with the overlying

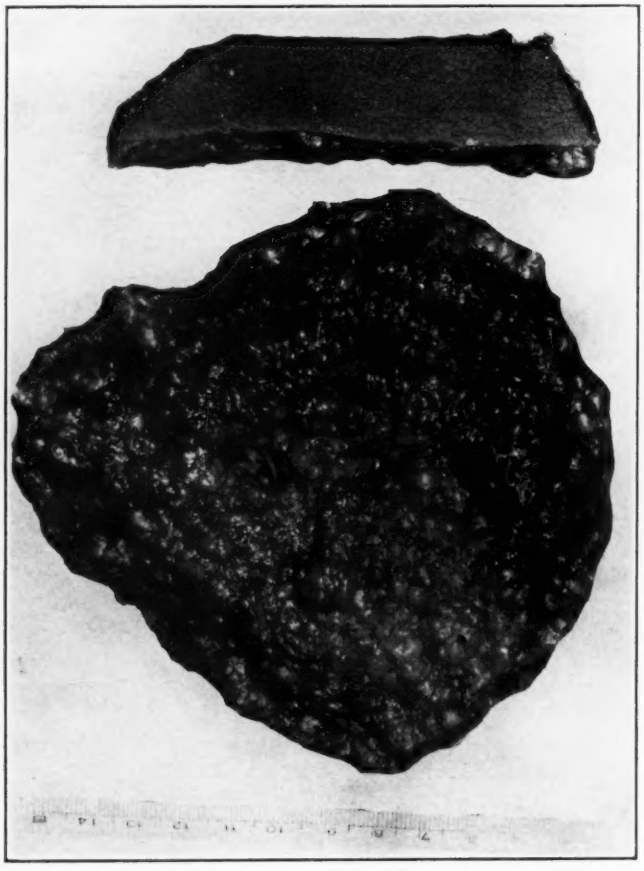

Fig. 3.—Lymphangioma of leg. Operative specimen showing large lymphatic spaces in the subcutaneous fatty tissue.

skin was excised. There was difficulty in distinguishing the limitations of the tumor from the surrounding fat, which could best be done by the difference in the consistency of the tissue when cut as the tumor was traversed by very fibrous trabeculae. The tumor extended down to but did not penetrate the deep fascia. The tumor had a rich blood supply and was made up of large spaces filled with clear fluid between fibrous trabeculae. Microscopically, it was composed of numerous endothelial lined spaces of varying size embedded in a dense acellular connective tissue. The tumor extended into the corium directly beneath the epithelium. In none of the sections was there evidence of angioblastic proliferation.

Angioblastoma.—Sabin has studied the manner in which angioblastic cells are differentiated from the mesoderm and how following proliferation solid cords of angioblastic cells are formed. Liquefaction takes place within these masses of cells so that a space filled with clear plasma is formed and lined by endothelium from the angioblastic cells. With this process in mind it is readily seen why some of the angiomas are chiefly made up of solid masses of angioblastic cells and why there may be a varying number of capillary, cavernous, or cystic spaces. It also explains why in the treatment of such tumors obliteration of the vascular channels may not be nearly as successful in producing a cure as in the former type.

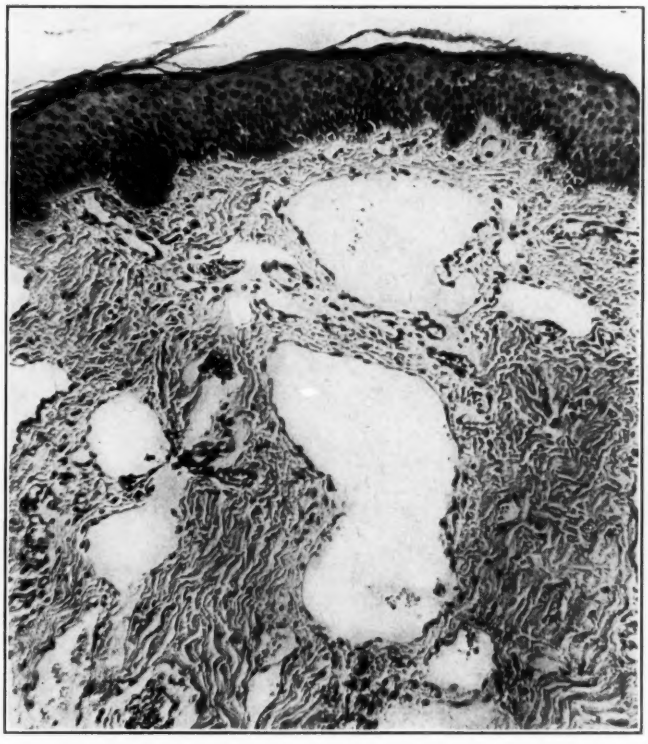

Fig. 4.—Lymphangioma of leg showing widely dilated endothelial lined spaces extending into the corium with no evidence of angioblastic proliferation.

These tumors may consist of numerous capillary or cavernous spaces with varying amounts of angioblastic cell proliferation. In other instances this proliferation predominates with masses of these cells and few vascular channels. Numerous cells in mitosis may be found indicating the active growth. This new growth extends and infiltrates the surrounding tissue and frequently compresses the vessels of the normal tissue. Because of the great variation in histologic structure, a multitude of names has been used to designate the types. These tumors have been called capillary or cavernous hemangioma, angiosarcomas, endotheliomas, etc. The most common of these histologic

varieties among the peripheral hemangiomas is the capillary type (Geschickter). In spite of the apparent malignant appearance of many of these tumors, it is rare for them to develop metastases and only by their local infiltrative growth do they destroy tissue or interfere with function of a part.

The treatment of angioblastomas of the extremities is similar to that employed for angioblastomas elsewhere. The best cosmetic results can be obtained by surgery if the tumor is small and the surrounding tissue loose. On the other hand, good results can be obtained by radiation, although on the extremities the effect of radiation on the surrounding normal vessels deserves more consideration than when the

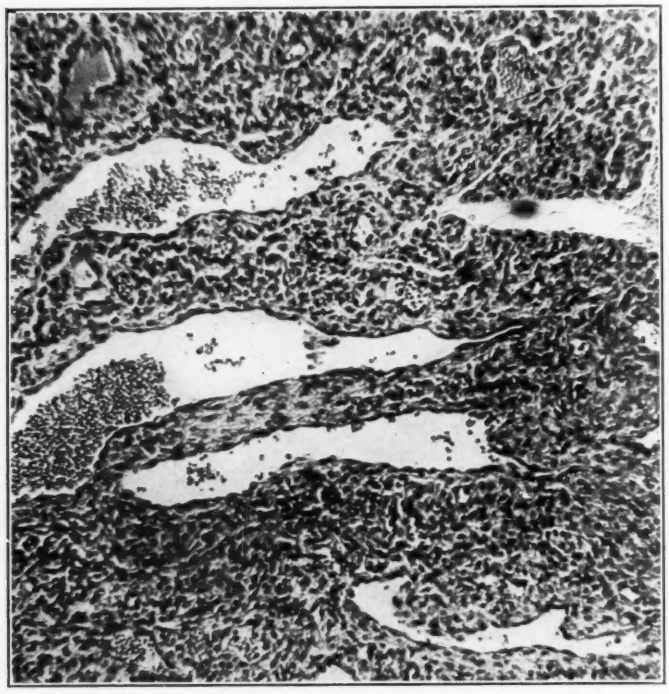

Fig. 5.—Angioblastoma. Note extensive angioblastic proliferation between vascular channels forming solid cords of cells in many places (×100), hematoxylin and eosin.

tumor is situated on the trunk. Sclerosing solutions also may be used successfully.

Lymphatic vessels may be the site of origin of angioblastomas. These usually consist of congeries of lymph vessels which tend to be dilated and which may form large cysts. Proliferation of the angioblastic cells as well as of lymph vessels may occur, although it is uncommon for this angioblastic cell proliferation to compose the major part of the tumor as is frequently seen in the hemangioblastomas. Malignant lymphangioblastomas are so rare that as Stout states: "There are many pathologists who have never seen (or at least never recognized) one."

Hemangioma of Skeletal Muscles.—Among the tumors occurring in the deeper structures of the extremities, and particularly in skeletal muscles, are hemangiomas. Because of their frequency and need for clinical differentiation, they are considered separately, although they in no way differ from angiomas elsewhere. Nearly 300 such tumors now have been described in the literature, approximately two-thirds of which have occurred in the extremities. They are nearly twice as common in the lower extremity as in the upper. They are more likely to be found in the larger muscles of the upper arm, thigh, and calf, but they have been reported as occurring even in the small muscles of the hand. The etiology of these tumors is not clear, but it is the consensus of opinion that the majority of them are probably congenital. They are more frequently encountered in the second and third decades of life, and nearly 95 per cent of all the tumors have been reported in patients under 30 years of age. The importance of trauma as an etiologic agent is open to question. There have been some cases reported in the literature (Mailer) which suggest that the tumor may have followed the trauma, but, on the other hand, there is always the possibility that there was a small tumor preexisting and the enlargement may have been due to hemorrhage following trauma.

Pathology.—The tumors are usually round or ovoid, varying in size from less than one to several centimeters in diameter. The histologic picture varies greatly, as it does in hemangiomas elsewhere. For the most part they are composed of rather large blood spaces with an endothelial lining and rather loose fibrous tissue. In some instances there may be such a marked proliferation of fibrous tissue as to lead easily to a diagnosis of sarcoma. However, they do not metastasize, and it is likely that the few instances of recurrence (6 per cent) have been due to incomplete removal.

Clinical Features.—The majority of these tumors are undiagnosed before operation. They are usually 4 to 5 cm. in diameter, situated deeply in the muscle. Some of the tumors are soft and compressible, while others are firm. Only rarely has the tumor been adherent to the skin. A considerable number have shown phleboliths on x-ray examination. Spontaneous pain is unusual, although there may be pain and soreness associated with exercise. In the larger tumors there may be limitation of movement and some loss of function. If the tumors are adjacent to the larger vessels or nerves, there may be atrophic changes. Occasionally there is a discoloration of the skin, sometimes dilated veins, and sometimes bruit.

Treatment.—The treatment of these tumors is surgical excision. Frequently the tumor infiltrates between the muscle fibers, which undergo degeneration, and it may be necessary to sacrifice a considerable portion of the muscle involved. While these tumors rarely if ever become malignant, they may increase in size, making total removal still more

difficult; hence early excision is indicated. It is important to recognize that these tumors occasionally may grossly and microscopically simulate sarcoma, and amputation has been needlessly performed.

Angioma of Bones, Joints, and Tendons.—Angiomas are among the less common bone tumors, and, while a considerable number are reported in the older literature, many of them were not true angiomas. The tumors are most frequently found in the second and third decades of life, although several have been reported in children. Frequently there is a history of preceding trauma. In the extremities they are usually near the ends of the long bones, although they have been seen in the midshaft. They are usually accompanied by a history of pain. There may or may not be a palpable tumor, and occasionally they have been described as soft or pulsating. The roentgenogram characteristically gives a multilocular or soap-bubble appearance with an expanding shell of paper thinness. Observation for a period may reveal that the tumor is extending in one direction only. The majority of these tumors have been described as cavernous, with little or no angioblastic tissue.

While these tumors are almost without exception nonmalignant, they, nevertheless, require treatment because of local extension and destruction of bone. They are usually successfully treated by curettage, cautery, or radiation.

Lymphangiomas and hemangiomas occur in and about joints and in tendon sheaths. These tumors may be congenital or may follow trauma. Occasionally these tumors are bilateral, indicating their congenital origin. They are usually accompanied by pain and boggy swelling, and the hemangioma occasionally pulsates. Some of these tumors following trauma are associated with a throbbing pain and vasomotor disturbances. Occasionally they may disappear spontaneously, presumably by thrombosis. The authors have seen one case in which the tumor followed a traumatic injury to the wrist. At operation profuse hemorrhage was encountered so that the removal of the tumor was given up. Following this the tumor disappeared, but the pain and vasomotor phenomena persisted and were relieved by a dorsal sympathectomy. The lymphangiomas of tendon sheaths and joints should be distinguished from degenerative cysts arising from the synovial membranes. The erosion of bone cannot be taken as evidence of neoplastic tissue, since the same phenomena may be observed in aneurysms and glomus tumor. The majority of these tumors would seem to fall into the group of angiomatous malformations.

ANGIOMYONEUROMA

This remarkable tumor has been recognized only in recent years and, owing to its unique histopathology, the severity of the symptoms and the physiologic importance of the glomus, it deserves special consideration.

Brief Review of the Literature.—The modern literature on glomus tumors dates from the observations of Barre (1920-1922), a French neurologist, and Masson, 1924, a French pathologist. However, it is evident that these tumors were recognized as clinical entities at a much earlier date, although under different names. As is frequently true, it is difficult to determine who first recognized these small, painful subcutaneous tumors as a clinical entity. The term "painful subcutaneous tubercle" was used by William Wood, of Edinburgh, in 1812 in describing a clinical syndrome which he had observed as well as collecting several cases from the literature. His description clearly indicates that most if not all of these cases of "painful subcutaneous tubercles" were angiomyoneuromas. However, only one of his cases occurred on the finger. Numerous other surgeons previous to this time were undoubtedly familiar with this small, painful tumor, among whom may be mentioned Campes, 1760; Morgagni, 1762; Cheselden, 1788; Bisset, 1792; Antoine Petit, 1799; and Dupuytren, 1835. With the advent of histopathology, further reports appeared (Kolaczek, 1877; Kraske, 1880; and others) and during this period they were usually classed as angiosarcomas. Muller in 1901 changed the name to "perithelioma" and Batigne and Gaudy (1901) to "fibromyomatous angioma." Other similar reports followed indicating that the tumor was being recognized as not a true sarcoma.

Barre in 1920 reported a case of a bluish tumor occurring underneath the finger nail associated with severe paroxysms of pain radiating up the arm to the neck and right side, associated with a Horner's syndrome and changes in the vasomotor reflexes. Excision of the tumor gave complete relief of symptoms. Barre gave this tumor, as well as others observed later, to Masson for study. Masson had obtained a similar subungual tumor in 1916. Stout summarizes his observation as follows: "He was struck by the fact that all three tumors had the same morphology and that all the patients had suffered from paroxysms of pain. He noted that the tumors were made up of a tangled mass of well developed arterioles, some with smooth muscle in their walls, all of which had peculiar 'epithelioid' cells arranged about their lumens. Moreover, the supporting framework of the tumors contained large numbers of nonmyelinated nerves, some of which were directly continuous with the cytoplasm of the epithelioid cells. All three tumors had large corpuscles of Vater-Pacini compressed and flattened out against their capsules, and these Masson felt must have been responsible for the pain. Believing that such a growth must represent the hypertrophy of some sort of an organ, because of its orderly arrangement and rich nervous connections, he examined serial sections of fingers, and came upon peculiar arteriovenous anastomoses which exactly resembled the structure of the tumors. These were found everywhere in the deeper layers of the skin of the

fingers, and in greatest numbers where the tactile corpuscles of Wagner-Meissner were present in the papillae. Somewhat similar structures had been described by Ruffini but without all the details noted by Masson, who could not be sure, therefore, that they were the same. Since this structure was a glomus (i.e., a conglomeration or plexus of minute arteries or veins) he felt it should have a distinguishing descriptive term and therefore called it a neuromyo-arterial glomus."

Since this time an increasing number of reports have appeared in the literature from all parts of the world, indicating that the tumor is probably of even greater frequency than at first supposed.

Arteriovenous Anastomosis. The Normal Glomus.—The histopathologic studies carried on by Masson and his associate, Popoff, have led to

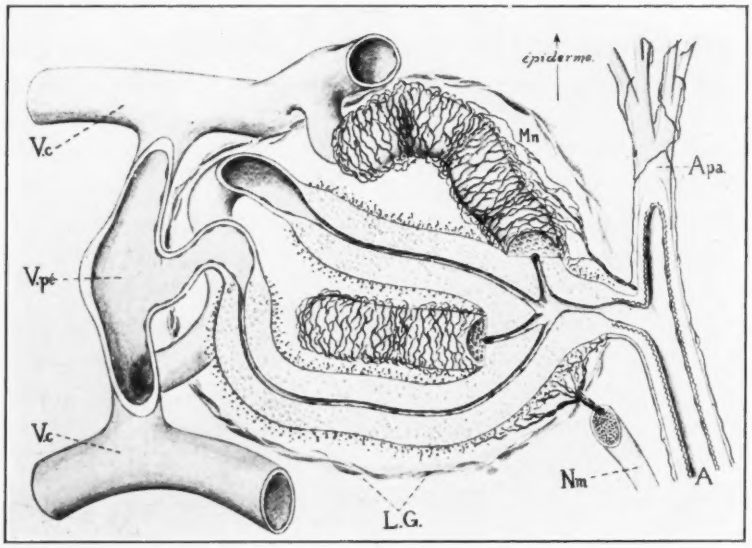

Fig. 6.—Schematic reconstruction of a glomus. *A*, Superficial preterminal artery. *Apa*, Terminal branch entering capillaries. *L*, The side branch is the afferent artery entering the glomus dividing into four neuromuscular arterioles. The elastica of the afferent arteriole disappears as soon as the arteriole enters the glomus. The wall of the vessel becomes thick due to an increase in smooth muscle fibers which terminate abruptly with the beginning of the venous segment. The efferent glomic vein leads into a collecting vein (*V.pe.*) which is dilated and thickened at the junction and in turn leads into the superficial veins, *V.c. Mn* is the rich perivascular network of nerves showing connections with the periarterial sympathetic nerves as well as myelinated sensory nerves to the skin. (After Masson.)

a renewed interest in the normally occurring arteriovenous anastomoses. The long-established concept that the blood normally passes from the arterioles to the capillaries to the venules has been so well established that it has been difficult to conceive of another normal means of communication between the arterial and venous systems. Nevertheless, as in the instance of the glomus tumors themselves, the existence of such a communication has long been known.

Müller in 1844 described direct connections between the arteries and cavernous sinuses of the penis. Subsequently, in 1862, he described direct connections between the arteries and veins of man in various

parts of the body. In 1877, Hoyer published a paper on "direct openings of very small arteries into vessels of venous character." Similar observations were made by Bourceret in 1855 and by Gerard in 1895 when the term arteriovenous anastomosis first appeared. A classical description of the histology of these anastomoses has been given by Grosser (1902). Space does not permit more detailed review of the numerous investigations of these interesting structures; for it the reader is referred to the excellent review by Eliot R. Clark. Arteriovenous anastomoses remained of academic interest until the work of Masson, since which time they have attracted the attention of physiologist, pathologist, and clinician. Masson linked the normally present arteriovenous anastomosis for the first time with a pathologic condition. In recent years several physiologists have studied the normal activity of these structures in the living animal. In 1930 Grant published his observations on arteriovenous anastomoses in the intact ear of living rabbits. He found that on heating the ear the arteries dilated at 35° C. and the arteriovenous anastomoses dilated at 40° C. He concluded that these structures are important in regulating body temperature. Clark, using a double-walled window in the rabbit's ear, has studied the activity and development of the arteriovenous anastomoses over a long period of time. He found that they exist in great numbers, twenty-five to fifty per square centimeter, and that their number may be greatly increased by exposure to trauma, temperature changes, or inflammation. In general, they behave in much the same way as arterioles, the chief difference being one of degree, for they are decidedly more active and show a greater tendency to independent action. "So rapid is the action of the arteriovenous anastomosis that it resembles a rapidly-acting stopcock." Clark states: "Regarding the function of arteriovenous anastomoses, the most one can say definitely is that, when dilated, they permit a large amount of blood to pass from artery to vein without passing through the capillaries. They undoubtedly play a part in the surface heating or cooling of the blood in the human hand and forearm and in the rabbit's ear, since they must allow a greater total flow through the exposed veins than would be possible without them."

Histopathology of Tumor.—The histopathology of the classical tumor is remarkably consistent. However, Clark has demonstrated the development of new arteriovenous anastomoses in the living animal and others have also shown great variations of these structures in fixed specimens. It is therefore not surprising that painful tumors composed of blood vessels which do not conform to the classical description are frequently found. The following description of the histology of the classical tumor is taken from Stout:

"The glomic tumors are composed of a tangled mass of blood vessels enclosed within a capsule. These vessels are lined with a single layer

of endothelial cells which are sometimes flattened and sometimes swollen. The endothelial layer is supported by a fibrous layer which may be quite thick but is usually exceedingly delicate, so that it can be seen only with silver or other differential fibrous tissue stains. The rest of the wall varies considerably in thickness and is made up of the peculiar cuboid or rounded 'glomus' cells (usually referred to as 'epithelioid' cells because Masson so described them) and smooth muscle, either well differentiated or in an embryonal form, in which the smooth muscle fibers are found within the cytoplasm of the epithelioid cells.

"The smooth muscle in some of the vessels, particularly those near the periphery of the tumors, is not infrequently in distinct bundles, which sometimes run parallel with the long axis of the vessel and sometimes tangential to it, but rarely completely surround its lumen. Usually there are epithelioid cells in the gap where the muscle is missing, and often there are epithelioid cells external, or internal, or both external and internal to the muscle bundles. Masson believes the vessels that are well provided with muscle are afferent to the glomus. The majority of the vessels, however, have no recognizable smooth muscle fibers either differentiated or undifferentiated.

"The glomus cells are quite distinctive. They have well defined cell outlines which are further accentuated by the presence of delicate collagen fibers which separate every cell from its neighbor. The cell cytoplasm is pale, emphophilic, and sometimes vacuolated, which brings into sharp relief the voluminous, centrally placed, globular or ovoid nucleus. It is a rare event to find a mitotic figure. Some of the glomus cells have short smooth muscle fibers within their cytoplasm.

"In the subungual tumors most of the vessels have small lumens containing rare erythrocytes. Outside of the nail bed the caliber of the tumor vessels may vary greatly, and some have dilated lumens similar to those seen in cavernous hemangiomas.

"The collagen fibers which form a meshwork between the epithelioid cells pass outward to join the stroma of the tumor which lies between the vascular complexes. This stroma is generally loose-textured and often shows mucinous degeneration (demonstrated by the mucicarmine stain).

"There are generally bundles of myelinated nerves in or near the capsule of the tumor which are recognizable with any stain. In addition, Stout has demonstrated, by the Gros and Rogers technique, the presence of numerous slender nerve fibers, seemingly without myelin sheaths, beneath the capsule especially and to a less extent in the stroma of the tumors. These fibers pass among the epithelioid cells which both Masson and Mason and Weil have shown are in direct continuity with the cytoplasm of these cells."

Clinical Features.—The distribution of angiomyoneuromas is almost entirely limited to the extremities, although an occasional case has

been reported on the trunk. Approximately two-thirds of the cases have been found in the upper extremity and one-third in the lower extremity. About one-third of the tumors have been subungual and nearly one-half of them have occurred in the digits.

The age of onset of the tumors varies from childhood to old age. The average age at which treatment is sought is in the third decade. The duration of the tumors varies enormously, from a few weeks to as long as thirty-seven years. This great variation in the duration is apparently dependent on the severity of pain and the ease with which a diagnosis is established.

The outstanding symptom associated with this tumor is pain. The occasional nonpainful tumor has been removed. Some of these tumors (Picard) do not develop spontaneous pain over long periods but are manifest merely as areas of increased sensitivity. The pain in the classical case is described as exquisite, agonizing, burning, throbbing, or bursting. The pain frequently occurs in paroxysms which may be initiated by pressure, changes in the weather, posture, or hot or cold water. At times there seems to be no reason for the paroxysms of pain. In some patients the pain may be so severe (see Case 2) and the radiation of pain so extensive that the localizing signs or trigger-point may be overlooked. The patient may wear a bandage or glove for protection, or in other instances the slightest pressure from clothing cannot be tolerated. Some patients obtain relief from pain by immersing the hand in ice water, while with others heat seems to be effective. Certain tumors may be emptied by slow pressure (Mason and Weil), following which there may be a disappearance of pain for hours. When the tumor is subungual, the patient may not allow the finger nails to be cut so that they grow to great lengths. Whether owing to the severity of the pain or associated vasomotor phenomena, sudden, unexpected trauma may result in an attack of fainting. The cause of the severe pain is obscure and, while it has been attributed to pressure on the pacinian body or adjacent nerve endings, a similar severe pain has been reported in arteriovenous fistulas (Livingston) without tumor formation. There are many instances of intractable pain having the same characteristics following trauma to the fingers in which no tumor could be found and amputation was the only treatment which yielded relief. Not infrequently these unfortunate patients are classed as various types of psychoneuroses and the problem deserves careful consideration from the standpoint of compensation. Changes in blood pressure frequently produce striking differences in pain. Relief may be obtained from elevation of the extremity or, if the blood pressure cuff is raised to diastolic pressure, there may be a great increase in the throbbing pain. On the other hand, if the veins of the extremity are emptied and the pressure abruptly raised above the systolic level, there may be an instantaneous relief of pain. There

is no conclusive evidence as to the pathways over which the pain is carried. Novocain block of the sensory nerves and of the sympathetic chain as well as periarterial sympathectomy have been done with only incomplete relief or change in the character of the pain. Radiation therapy is ineffective (Adams, Stabins, and others) and even after complete excision local sensitivity may remain for long periods before it finally disappears.

The signs associated with angiomyoneuromas are variable depending on the location, size, and depth of the tumor. Local tenderness is the most consistently present sign. The degree of color in the tumor depends on its size and depth. Usually a change in color is discernible and frequently it is marked. The majority of the tumors are described as blue or purplish and a few are red. Others exhibit color changes associated with vasomotor phenomena. The subungual tumors may or may not exhibit a color change as seen through the nail and frequently exist for years with no discernible color changes of the nail other than a very faint cyanosis. Inasmuch as the bulk of these tumors is usually composed of blood vessels, they frequently are not palpable unless located superficially. The size of the average tumor varies from 3 to 5 mm. and only rarely have tumors 2 to 3 cm. been reported.

Roentgenographic examination of the tumor is always worth while, particularly when the tumor is adjacent to bone. The tumor, because of its pulsatile character when in contact with bone, frequently erodes through the cortex in the manner of an aneurysm. A recent report of Bergstrand, of Stockholm, suggests the possibility of the origin of some of the tumors within bone, although this is not definitely established.

Vasomotor phenomena may or may not be associated with these tumors. Those tumors arising in the digits seem more likely to be associated with sympathetic nervous system manifestations. As a rule the involved extremity is distinctly warmer than the normal side. It has also been shown (Stabins) that recovery from exposure to cold is more prompt in such an extremity. These changes are not limited to the involved digit but involve the entire extremity and may extend to the trunk and face as unilateral sweating. Occasionally in the more painful variety a unilateral Horner's syndrome is seen, usually manifest during a paroxysm of pain. There may also be other associated reflex changes. In severe cases of long duration these phenomena may persist for months or years after removal. An increase in the pulsation of the palpable arteries may be discernible which is best demonstrated by oscillometric readings and which may be as much as double the normal extremity.

A variety of atrophic changes may be demonstrable in the involved extremity and may lead to a mistaken diagnosis of a central nervous system lesion (see Case 2). These atrophic phenomena may be brought

about by the atrophy of disuse and vasomotor changes, or both. Atrophy of the musculature seems to be chiefly a disuse phenomenon. Skeletal postural changes may result from carrying the extremity in a certain position in order to obtain relief from the pain. A soft, wrinkled, thin skin associated with the extreme hyperhidrosis may be present. In the subungual tumors the nail may be curved and thickened with longitudinal striations associated with slow growth, probably owing to interference with the nail matrix. In cases of long duration these changes may be permanent or require years for their disappearance.

Differential Diagnosis.—It has been previously stated that pain (induced or spontaneous) and local tenderness are the most constant symptoms of angiomyoneuroma. Other tumors occurring in the nail bed, owing to the close association with the great number of nerve endings in this region as well as the fact that it is a semiclosed space, may give similar symptoms. This suggests that the peculiar vasomotor phenomena associated with the angiomyoneuromas may not be due primarily to these tumors but to their location and associated nerve structures. However, the diagnosis of other similar tumors occurring in the literature, such as fibroma, etc., previous to the clinical-pathologic demonstrations of Masson, should be regarded with suspicion.

Fibroma.—Certain cases of fibrous tissue tumors have been reported (Dubring, Chandelux) which have had similar clinical features.

Angioma.—Occasionally cases are encountered presenting the clinical features of angiomyoneuromas which on removal fail to show all the typical features of the glomic structure. It is possible that these are similar tumors which for various reasons (incomplete development or technical) fail to show the classical structures.

Exostosis.—These are not infrequently painful and sometimes discolored. The roentgenogram readily yields the diagnosis.

Sarcoma.—While many of the sarcomas in the older literature have undoubtedly been angiomyoneuromas, true sarcomas occasionally occur.

Carcinoma.—The subungual carcinoma is rare, but a few cases have been reported.

Melanoblastoma.—The differential diagnosis of a tumor appearing underneath the nail must include malignant melanoma; first, because of the extreme importance of an early diagnosis and radical treatment; and second, because it is one of the common subungual tumors. These may follow injury and occasionally are painful, but usually the pain is a minor symptom. Ulceration is more common and pigmentation a more striking feature.

Other lesions which should be considered are subungual corns, papillomas, enchondromas, angiokeratomas, and Boeck's sarcoid.

Angiomatous Leiomyoma.—Solitary cutaneous and subcutaneous leiomyomas should be mentioned among the vascular tumors of the ex-

tremity; first, because some of them certainly arise from the smooth muscle of blood vessels; and second, because they may simulate the painful syndrome of the glomus tumor and have been included with these tumors in the older literature under the term "painful subcutaneous tubercle." Stout has presented an excellent review of these tumors to which the reader is referred for details.

The frequency of these tumors appears to be about the same as the angiomyoneuromas, as nearly one hundred cases have been reported. The leiomyomas, unlike the angiomyoneuromas, do not seem to be associated with any particular structure and may arise from smooth muscle anywhere in the skin and subcutaneous tissue. It is frequently difficult or impossible to determine their exact origin, but it is likely that nearly one-half of them arise from the smooth muscle of blood vessels. There has been considerable discussion as to whether they arise from arteries or veins and there are no tumors reported arising in the larger arteries. It seems remarkable that they should arise only in the veins, but such seems to be the weight of evidence. Nearly one-half of the tumors occur on the extremities, particularly the extensor surfaces. Unlike the glomus tumor, they are relatively uncommon on the digits and occur with greater frequency in the legs.

The clinical appearance and behavior of some of these tumors may be very similar to the angiomyoneuroma. They are usually of small size (2 to 15 mm.), although, unlike the glomus, they may reach several centimeters in diameter. Occasionally the tumor is pedunculated, but usually it is in or underneath the skin. The tumor is usually colorless but occasionally has been described as varying shades of brown or red, and in a few instances as bluish. The tumor usually is painful or tender (twelve of fifteen, according to Stout). Occasionally the pain may be paroxysmal in character with radiation similar to that in the glomus tumor. However, as a rule, the pain is less severe and less likely to be paroxysmal in character. The cause and mechanism of the pain are not clearly established. However, contraction or wormlike movements have been observed during a paroxysm of pain and some tumors have been seen to contract after removal. These tumors occasionally undergo malignant change with metastasis to lymph nodes, bone, and viscera. A history of preceding trauma is sometimes obtained, but there seems to be no established relationship between trauma and tumor formation.

The treatment of choice of these tumors owing to their small size is surgical excision. However, they have been removed by various agents, such as caustics, electrocoagulation, and x-ray.

CASE 2.—No. A1692. G. B., an Italian, 28 years of age, entered the New Haven Hospital complaining of a sensitiveness and burning sensation of the left thumb and hand. He attributed his difficulty to the intraspinal injection of diphtheria antitoxin at 12 years of age, following which he developed pain in the left thumb and

hand with a slight discoloration of the nail. The pain and hypersensitivity had slowly increased since that time. For a number of years he had been able to carry on by avoiding trauma to the thumb. In 1925 he entered the Neurological Institute of New York City where he remained for three weeks. At this time he complained of a burning pain in the left thumb which kept him awake. When he sucked the thumb, the pain shot up the thumb, sometimes skipping the arm, and was felt in the left lower jaw. He also complained of excessive perspiration of the left hand. At times there was a burning of the tip of the little finger and in the second phalanx of the ring finger of the left hand. He described this as if something were forcing its way through his fingers. He stated that his symptoms had been of some years' duration, had progressed slowly, and were worse in winter than in summer. Neurologic examination revealed the skin to be deeply pigmented with several brownish patches such as are found in von Recklinghausen's disease. The deep reflexes were equal and hyperactive, and sensation was normal. The left arm was smaller than the right. The left wrist was like that of a girl's, smaller than the right; and the left hand was the loose, thin, flexible hand of a girl, while the right hand was strong and thick. The left thumb and nail were much smaller than the right. The thenar and hyperthenar eminences were somewhat atrophic on the left. The left thumb nail was thicker and harder than the right. It was noted also that he was of the thin feminine type with the tendencies above noted, and that his voice was high-pitched. Laboratory work was entirely negative; x-ray examination was also negative. It should be noted that the skeleton was x-rayed, except for the left thumb, which was off the film. It was thought that some generalized atrophic disturbance accounted for the slight lack of normal development. The diagnosis was a constitutional ectype and the case was regarded as a pathologic curiosity. In 1928 the patient entered St. Raphael's Hospital, New Haven, where he was operated upon. A rather extensive sympathectomy of the brachial artery was performed. There was no improvement whatever after the operation.

The symptoms continued to grow worse and on April 25, 1934, he entered the New Haven Hospital where the following additional history was obtained. For the past ten years the thumb had become increasingly sensitive. There seemed to be two types of pain, one of which was of the steady, burning character and frequently would awaken him at night, and for which he obtained relief by placing his hand in ice water. The other was a more severe, stabbing type of pain as the result of a blow or when clipping the nail. For years he had cut his nail only with a very sharp razor blade. The pain was worse with a change in weather; also, severe exercise, such as running, would increase the pain. He had noticed that his left hand was always hot and whenever the pain was severe there would be very profuse perspiration. At times the pain would radiate throughout the entire arm, involving the shoulder and side of the face.

Physical examination was essentially negative except for the condition of the arm. The entire arm and hand were smaller than the right. Measurements were as follows:

	RIGHT	LEFT
Biceps	26 cm.	23 cm.
Forearm	25 cm.	22 cm.
Wrist	17 cm.	15 cm.
Hand	21 cm.	17 cm.

The blood pressure of the left arm remained consistently 10 to 15 mm. above that of the right. There seemed to be no demonstrable weakness of any particular muscle group although the entire thumb and hand were somewhat weaker than the right. The skin of the palm of the hand was constantly moist and seemed to be definitely

Fig. 7.—Showing atrophy of entire hand as well as thumb.

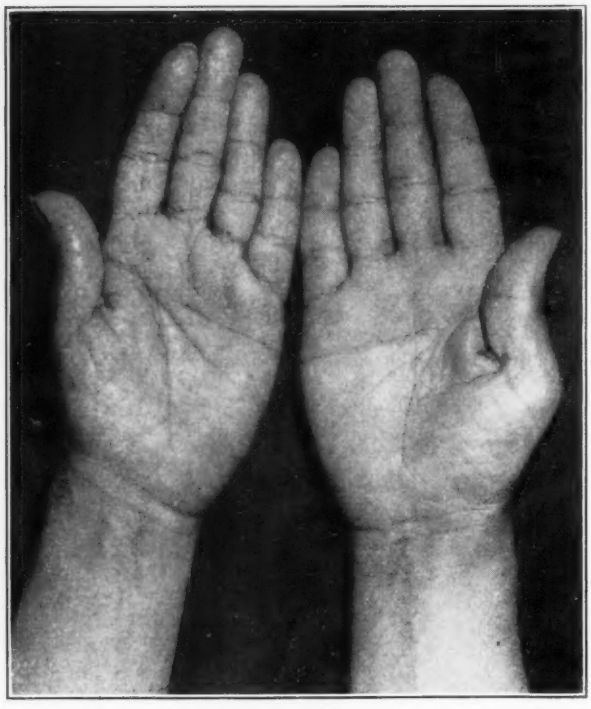

Fig. 8.—Showing atrophy and thin wrinkled skin of palm.

thinner than on the right and was profusely wrinkled. The anterior surfaces of all of the fingers were more sensitive than those on the right. The thumb was exquisitely sensitive over the distal phalanx and the slightest tap with the head of a pin over the palmar surface or over the base of the nail of the left thumb was excruciating. The patient fainted on accidentally striking the thumb. The left thumb was somewhat narrower than the right and showed increased longitudinal ridges. There was a faint bluish discoloration over the base of the nail. Temperature studies showed that the left hand was at a full vasodilation level with the temperature at 96° with a room temperature of 68° over a period of several hours.

A novocain block of the dorsal sympathectomy was performed on the left. Inasmuch as the hand was at a full vasodilation level, no information could be obtained from this source. However, as the hand was continually sweating and following any painful stimulus to the thumb there was a steady drip from the finger

Fig. 9.—Showing atrophy of thumb and longitudinal striation of nail.

tips, this afforded a very good means of determining the effectiveness of the novocain block. Within ten minutes after injection of the novocain, the hand was completely dry, the burning pain and hyperesthesia disappeared, and pain could be elicited only on pressure over the thumbnail.

Roentgenographic examination of the left hand revealed a generalized decrease in the size of all of the bones of the left hand and that portion of the radius and ulna visualized. The osseous structure of all the bones was normal except for the thumb which revealed irregular cystic areas of varying sizes with a coarsening of some of the trabeculae and also an indistinct outline of trabecular markings on the superior and lateral aspect suggestive of destruction. The pathology was confined chiefly to the top and distal portion of the shaft of the terminal phalanx where there was complete destruction of a small area. Roentgenographic impression: primary bone tumor of the terminal phalanx of the left thumb with areas of cystic degeneration.

Oscillometric readings of the left upper arm were only slightly greater than on the right; however, oscillometric readings of the left forearm were nearly twice those of the right.

At operation on May 9, 1934, the nail was incised across the base and removed. Showing through the subungual epithelium was a small, bluish, discolored area. The subungual epithelium was incised longitudinally over the tumor and a flap reflected. This gave a good exposure of the tumor which was extremely vascular. The tumor was readily removed by blunt dissection and although it had scalloped out the terminal phalanx in no place was it adherent. The tumor measured 5 by 4 by 3 mm. A large artery was found to enter the tumor on its anterior surface. Pathologic examination revealed the classical histology as described by Masson.

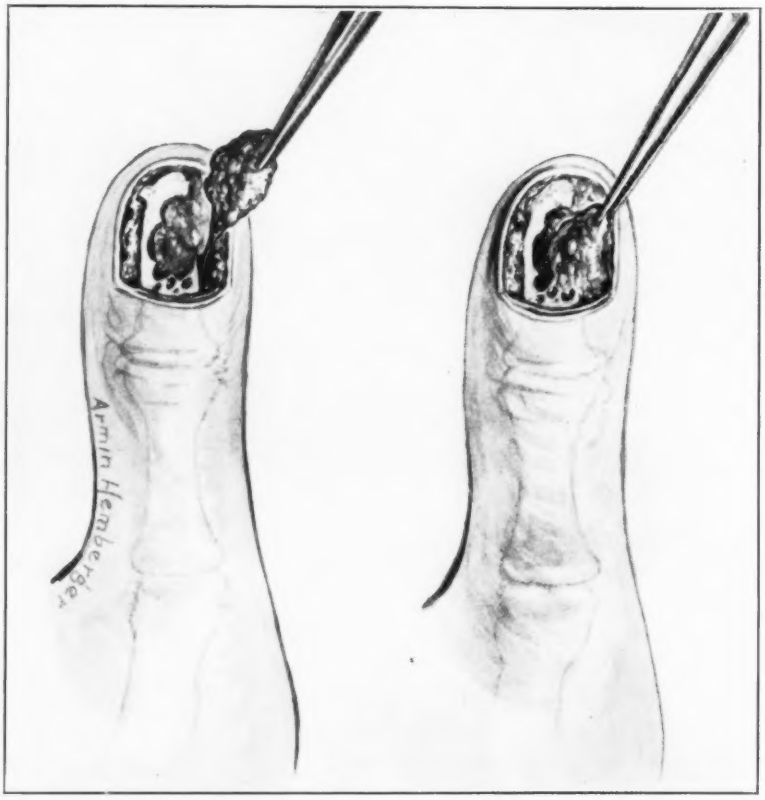

Fig. 10.—Sketch of tumor as seen at operation showing erosion of bone.

Postoperative Course: Although four years have elapsed, during which time the patient has been free from symptoms, there has been only slight improvement in the atrophic appearance of the skin and musculature of this hand. In spite of efforts at reeducation the patient does not use his hand with as much freedom as he normally should. It is possible that part of the failure to overcome the atrophic defect may be due to disuse. There is still a slight tendency for this hand to perspire more freely than the normal side.

This case illustrates the extreme radiation of the pain and the profound atrophic developmental changes in muscle, bone, and skin. The relief during the novocain block suggests that the burning, throbbing

type of pain is carried over the sympathetic nervous system, while the failure to obtain relief following the brachial periarterial sympathectomy demonstrates that these fibers leave the artery below this point.

IDIOPATHIC MULTIPLE HEMORRHAGIC SARCOMA (KAPOSI'S DISEASE)

Idiopathic multiple hemorrhagic sarcoma is a rare condition, which, however, is not uncommon in the larger centers with a cosmopolitan population. Dorffels in 1932 found 356 cases in the literature, but this is hardly representative of the incidence since cases are no longer reported unless they present unusual features. A study of the age distribution in this series shows the highest incidence in the sixth and seventh decades. The disease occurs predominantly in males with a ratio of 15 males to 1 female in Dorffels' series. The disease is especially prevalent in men of Italian and Galician birth (MacKee), but, as Dorffel points out, it appears to have a geographic rather than a racial distribution, since the vast majority of cases originate in Russia, Poland, and Northern Italy. Cases, however, have been reported from practically every civilized nation in the world. Another striking feature is the great prevalence of the disease among the laboring classes.

Clinical Manifestations.—The disease has a tendency to develop first on the extremities as a unilateral lesion, but during its course it usually becomes bilateral and frequently symmetrical. The disease may be generalized, involving the viscera as well as the cutaneous tissue, but as a rule the first lesions are cutaneous. The eruption is a progressive one which may develop slowly over a period of years with lesions undergoing spontaneous regression, leaving atrophic pigmented scars. The lesions are usually superficial, localized in the skin. The typical lesion is characterized by nodules and plaques of a blue, blue-red, or red-brown color. The lesions vary from 0.2 to 1 or 2 cm. in diameter and are usually multiple. As the disease progresses, coalescence of a number of lesions may result. This may become so extensive that swelling of the extremities approaching an elephantiasis may develop. There is little tendency for ulceration although fungous infection of the overlying hyperkeratotic dermis may occur.

Other lesions which simulate vesicles or lymphangiomas have been described, as well as rapidly growing angiomatous lesions which resemble simple angiomas or granulomapyogenicum. The skin lesions as a rule give rise to few subjective symptoms, although itching of the skin is the most common complaint. Occasionally the lesions have been associated with severe pain.

The disease progresses slowly with periods of intermission. The average duration of life is between five and ten years. Death is usually due to intercurrent infection or some complication resulting from extensive visceral involvement.

Histopathology and Pathogenesis.—While the pathogenesis of the disease is entirely obscure, the histologic characteristics of the disease are well known. MacKee and Cipollaro have described the lesion in detail as follows: "Three pathological processes are recognized (1) inflamma-

Fig. 11.—Kaposi's disease, showing plaque-like lesions with many coalescent on extremities (note elephantiasis-like swelling of legs).

tory; (2) granulomatous; (3) neoplastic. Very often these processes overlap and produce a borderline or mixed picture.

"When the *inflammatory process* predominates the cardinal features are (a) dilatation of blood vessels and lymphatics; (b) perivascular in-

filtration of mixed cells—round cells, connective tissue cells and some plasma cells; (c) edema, hemorrhage and iron-containing pigment.

"When the *granulomatous element* is accentuated, the predominating features are (a) proliferation of small blood vessels and also lymphatic vessels; (b) proliferation of connective tissue with young nucleated cells predominating and perivascular infiltration of mixed cells; (c) edema, hemorrhage and iron pigment.

"When the *neoplastic features* predominate the picture varies with the element involved (a) when the changes are principally vascular, the picture may be that of an angioma or may resemble granulation tissue or granuloma; (b) when the lymphatics are involved, the picture may suggest lymphangioma or a mixture of angioma and lymphangioma; (c) when the connective tissue proliferation predominates, fibroma, angiofibroma, angiosarcoma or spindle cell sarcoma may be suggested.

"These lesions are confined primarily to the derma. Changes in the epidermis are secondary and are not pathognomonic nor important. The subcutaneous involvement is usually secondary as a result of extension of the process along the blood vessels."

While these various lesions may be found at different stages of the disease, and some elements of each found in even the more advanced processes, the earliest lesions present predominantly an inflammatory appearance.

A variety of ideas have been expressed as to the pathogenesis of the disease. Pautrier and Diss feel that it is a neurovascular dysgenesis and a pseudosarcoma, on the basis of one case in which they found cellular derivatives of vascular neuromuscular adnexa and Schwann cell elements. Dorffel feels that the disease is primarily one of the reticuloendothelial system which may terminate in malignancy, although he is not willing to call it a reticuloendotheliosis. MacKee and Cipollaro, after careful review of their own material as well as published data, feel that some "unknown systemic agent" attacks the vascular apparatus, causing chronic hyperplastic inflammation and granuloma, and that its histogenesis is compatible with and indistinguishable from that of a malignant new growth or neoplasm. Attempts at transmission of the disease by animal inoculation of suspensions of tissues have yielded negative results, although Justus claims to have produced lesions in rabbits and carried them through several generations.

Differential Diagnosis.—The clinical diagnosis is readily established by the progress of the disease, although at various stages it may simulate syphilis, sarcoid, mycosis fungoides, leprosy, and lichen planus. The histologic pathology of the disease is so characteristic, if lesions at various stages of development are examined, that a differential diagnosis is

easily made. It is important, therefore, to examine several lesions because one alone may be misleading.

Treatment.—Most authorities agree that roentgen therapy offers the best results, although recurrence is likely sooner or later. Most of the lesions, as well as symptoms of pain and itching of the skin, disappear promptly with x-ray. MacKee advises repeated small doses of about 75 r. administered once a week to the area of involvement. These may be continued for ten to fifteen weeks. If the lesions are small, larger doses may be used. Small lesions respond equally well to radium. Arsenic administered by mouth, either as Fowler's solution or Asiatic pills, or subcutaneously, intramuscularly, or intravenously, has been used, but it is considered of questionable value at the present time. Small lesions can be cured by surgical removal. Several cases of disappearance of the lesions following treatment have been reported, although it must be emphasized that the disease is a slowly progressive one and that the follow-up on none of these cases has been sufficiently long to consider them cures.

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TUMORS OF THE SYNOVIA, TENDONS, AND JOINT CAPSULES OF THE HANDS AND FEET

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A LARGE portion of the soft tissues of the hands and feet consists of tendons, their synovial sheaths, and the joint capsular tissues. A variety of both benign and malignant tumors arises from them, but, with the exception of the so-called ganglion, such neoplasms are not common. In general, the benign tumors appear quite circumscribed, and, when not very large, their close association with a tendon, sheath, or joint capsule is readily surmised upon clinical examination. A history of slow growth and variability of pain and tenderness are characteristic of benign processes. Benign tumors may interfere with function when so situated, or when they attain large enough size to prevent the free gliding of tendons through their sheaths or beneath annular ligaments, or when there is mechanical obstruction to full range of motion of a joint. On the other hand, they may extend about the sheaths and tendons, producing large soft masses without causing functional impairment.

Differential diagnosis from acute infectious processes in the tendon sheaths usually is not difficult. In the latter there is, of course, rapid onset, fever, severe pain, sometimes superficial evidence of acute cellulitis, and often a history of a recent wound. Differentiation from chronic inflammation may be more difficult in some cases. In such inflammations an entire sheath is involved; whereas, in the case of a neoplasm the process is usually well circumscribed. Inflammatory thickenings tend to be soft and "fleshy"; whereas, most tumors, except for lipomas, are more firm. Diffuse chronic inflammatory changes in the synovia of the hands and feet sometimes may be a localized manifestation of a generalized arthritis. In differentiation from tuberculous synovitis the following points favor the latter: (1) Sensory or functional symptoms may precede the development of swelling (Mason[1]); (2) the soft swelling may be of sudden onset and may progressively follow the course of the sheath; it usually is first apparent at the wrist; (3) rice bodies (osteochondromatosis may give rise to a similar palpable sign); (4) greater functional disturbance than usually caused by tumors.

Roentgenographic examination of the hand and foot is also of value in the differential clinical diagnosis. The soft tissue shadows cast by such neoplasms serve to indicate to some extent their deeper exten-

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sions. Because of the marked difference in absorption of rays by fat, as compared to the other tissues, it should be possible to make a roentgenographic diagnosis of lipoma when this is not certain from clinical inspection. Secondary involvement of bone, such as obtains in certain cases of xanthomas arising near the insertion of tendons or in joint capsules, also may be demonstrated. Osteochondroma and osteoma of the tendons and sheaths afford characteristic shadows but must be differentiated from sesamoid bones.

Ganglion.—This is a common condition of the hands and feet, observed most often on the dorsal aspects of the wrist (Fig. 1). Other frequent sites are the dorsal aspect of the ankle, foot, and palmar surface of the wrist. They may also arise from tendon sheaths and in rare instances in tendons themselves. They form firm smooth rounded

Fig. 1.—Oval and flattened cystic mass on the dorsum of the wrist. At operation this proved to be a ganglion arising from the underlying extensor tendon sheaths.

masses which upon palpation yield the sensation of fluid under pressure. It is generally held that these lesions are not herniations of the synovia but the result of fibroplasia in which isolated areas of colloid degeneration appear, which in turn coalesce to form a large uni- or multiloculated cyst filled with clear viscous fluid.[2] Microscopic examination of the wall reveals it to be composed of dense fibrous tissue and the lining of the larger cystic spaces sometimes resembles synovia with an occasional villus (Fig. 2*A*). Foci of myxomatous changes may be present in the wall, especially the base (Fig. 2*B*).

That trauma may be an etiologic factor is suggested by the fact that ganglions are often observed in persons who use their hands a great deal, such as typists, musicians, etc.

Conservative treatment consists in striking the mass with a hard flat surface, such as a book or board, in order to collapse the principal

cystic spaces. Aspiration of the viscid fluid with reinjection of a drop or two of iodine, phenol in glycerin, or sodium morrhuate followed by a compression bandage is another form of conservative management.

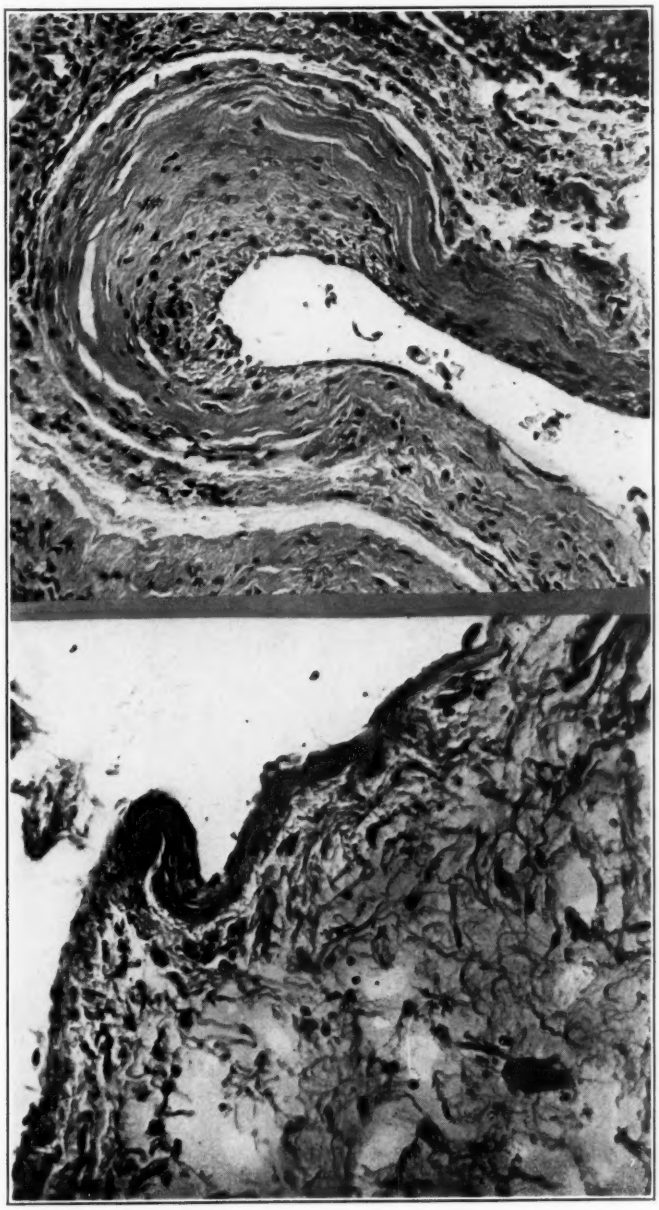

Fig. 2.—Showing various histologic appearances of the walls of ganglia of tendon sheaths and joints. *A*, Photomicrograph (×200) of dense fibrous wall, mature cells, and some "pavement" cells lining the cavity; *B*, photomicrograph (×250), showing definite lining of cavity and myxomatous-like tissue in the wall.

Bearse[3] recently has stated that the aspiration treatment is more effective if a large gauge needle is employed to permit thorough drainage of the fluid contents.

The treatment of choice is generally conceded to be excision. A transverse or longitudinal incision is made over the mass and the latter excised in toto if possible. Where there is a broad attachment at the base, the ganglion is usually punctured during the operation. Closure of the wound is performed without drainage. Recurrences are not rare due to incomplete excision, especially of the base.

Large complex, multiloculated ganglia with rather extensive development about sheaths and tendons have been described. Compression of fluid from one portion to the other is a characteristic sign. The treatment is excision, which may necessitate large incision and careful extensive dissection to free the structure in toto.

Fibroma.—These lesions are rare in close association with the tendons, sheaths, and joint capsular tissues of the hands and feet.[4] They form small, firm, well-circumscribed nodules which may or may not be tender. Their true nature cannot be finally determined until examined microscopically since clinically they are not distinguishable from other tumors of these structures.

In some instances "snapping" digits are the result of small rounded or fusiform dense fibrous masses in the tendons, and, when at operation the area is exposed, these growths may be shelled or cut out of the tendon and the latter thus reduced in size to permit normal function.[5]

Multiple or single superficial or deep fibromas may be observed in the hands and feet as part of a generalized neurofibrinomatosis of von Recklinghausen. I have observed two such cases in adults, in one of which a large fleshy mass was removed from the deep palmar space for cosmetic purposes, the growth having been present since childhood (Fig. 3).

Xanthoma or Giant Cell Tumor of the Tendons and Sheaths.—The question of whether these processes represent true neoplasms or are a local manifestation of some obscure disturbance in fat metabolism has not yet been settled.[6] They are observed in patients of all ages, and usually grow slowly. Pain or tenderness is absent or not a prominent symptom. They occur more often in the hands than the feet. They form moderately soft or firm rounded, coarsely nodular masses in the digits near tendinous insertions (Fig. 4), from which points they arise or they may be firmly attached to the wrist or ankle joint capsules, or they may develop extensively about the flexor or extensor tendons arising primarily in the sheaths. Secondary invasion of bone with limited destruction of the latter has been observed in some cases where these neoplasms arise from tendinous insertions or bony attachments of joint capsules. In some cases xanthelasmas of the skin in other parts of the body[7] and hypercholesteremia may be associated with these tumors.

The gross appearance is mottled yellow, yellow-brown, and gray, and this is quite characteristic. Histologic examination (Fig. 5) re-

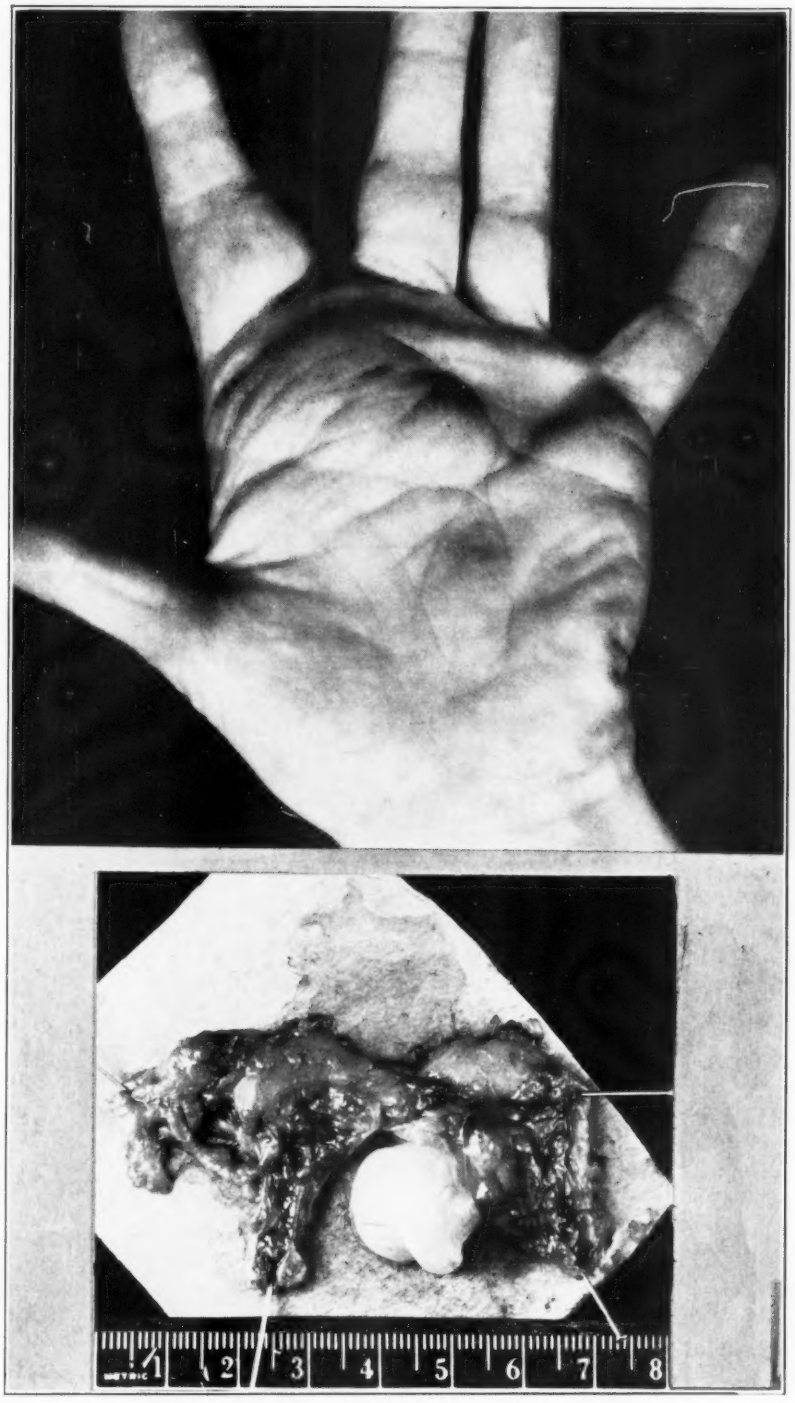

Fig. 3.—*A*, Fleshy tumor of palm of hand and base of index finger, present since childhood, and a localized manifestation of generalized von Recklinghausen neurofibromatosis. There was no functional impairment. *B*, Photograph of excised specimen showing plexiform neurofibroma with one definite myxomatous portion (the white mass attached to lower margin).

Fig. 4.—Coarsely nodular tumor on palmar aspect of ring finger of left hand, two years' duration, in 44-year-old white female. At operation, through small linear incision along outer margin of palmar aspect of the swelling, a brownish soft mass was easily shelled out and found to arise from the flexor tendon sheath. Microscopic examination: xanthoma.

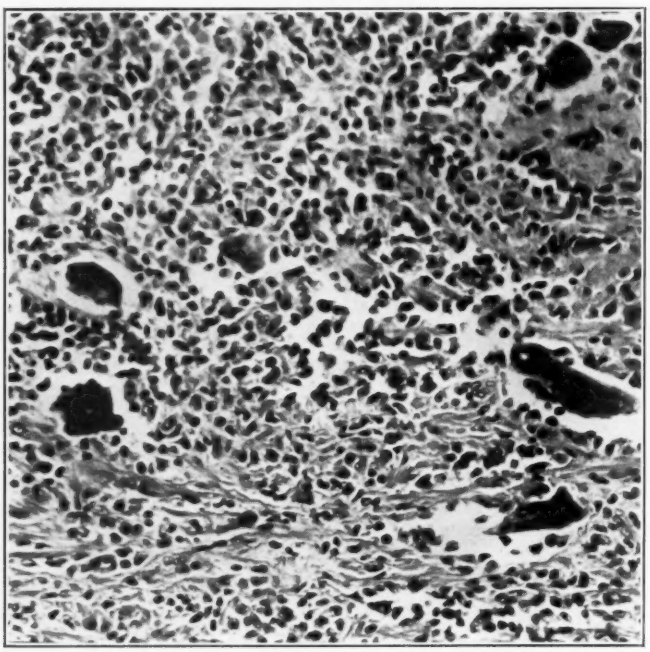

Fig. 5.—Photomicrograph (×270) of portion of xanthoma or giant cell tumor of tendon sheath shown in Fig. 3. Note foreign body giant cells and stroma of rounded and spindle cells.

veals a groundwork of dense fibrous tissue in which are scattered spindle and rounded cells, foreign body giant cells, sparsely distributed or in large numbers, and aggregates of large lipoid containing foam cells, macrophages with brown pigment, and sometimes cholesterol crystals. In a few instances the stroma contains islands of cartilage and even a few bony trabeculae.

Treatment: Excision is advised because of cosmetic, functional, or other reasons, and, as soon as the masses are exposed through limited incisions over them, their true nature is apparent because of their color. When not large they tend to bulge through the incisions of access and may be easily removed. A small pedicle of attachment to sheath or tendinous insertion is often found and in the latter attachment secondary invasion of bone may be present. This is removed by curettage. Extensive spread about the tendons may require large incisions and careful and prolonged dissection for removal. Recurrences are rare but occur presumably from fragments of the process left behind.

Prognosis: Since the tumors are benign, the prognosis is good.

Lipoma.—While the larger joints such as the knee, shoulder and hip, are the common sites of synovial lipomas, they also, in rare instances, occur in the association with the sheaths of the hands and feet, forming soft or moderately firm compressible masses which have slowly increased in size. Of 34 cases in the hands reviewed in the literature by Straus,[8] only 1 was recognized as such before operation (Filho). They develop as lipomatous or fibrolipomatous bodies within the tendon sheath or about it. In the hands they may be confined to the fingers, extend for some distance along the tendons, or be confined to the level of the midpalmar space. They may be symmetrical in both hands. In Straus' case of lipoma of the flexor sheath of the fourth finger arising at its palmar terminus, the mass extended backward under the palmar fascia into the interdigital spaces on either side of the fourth finger and in dorsal direction along the lumbrical tendons on either side of the finger to produce a bulge on the dorsal aspect of it. Excess pads of fat developing about the malleoli in one or both ankles are sometimes considered to be lipomas. Gosselin suggested that lipomas change from a soft to a more firm consistency when their temperature is substantially lowered by application of an ice bag. Straus confirmed the clinical value of this test.

Grandclaude, Razemon, and Bizard[9] reported a spectacular case of arborescent angiolipoma of the flexor pollicis longus tendon, which, after its presence had been noted for several months by the patient, apparently produced a spontaneous rupture of the tendon.

Treatment: Excision of lipomas of the tendon sheaths is performed often through limited incision because when overlying pressure is re-

lieved they tend to bulge into the field. On the other hand, minute ramifications may necessitate extensive and meticulous dissection to avoid injury to nerves, tendons, and vessels. Regardless of size or complex structure, lipomas of the tendon sheaths usually have rather limited pedicles of attachment. It is important to identify and completely excise these pedicles as well as all portions of the tumor because incomplete excision may in time be followed by recurrences.

Osteochondroma and Osteoma.—These growths are among the rarer ones observed in the tendons, sheaths, and joint capsules of the hands[10] and feet,[11, 12] but are not so very rare in the larger joints, such as the knee, hip, elbow, and shoulder. While in the latter locations they are usually multiple in the joint synovia and sometimes regarded as metaplasia on an inflammatory basis, those few observed in the hands and feet are considered to be true neoplasms.

While often referred to as situated in the tendons, in most instances described in the literature operation revealed a primary pedicle of attachment to the sheath frequently near the osseous insertion of the tendon. Tenderness and some swelling may be present, especially following exercise of the part, and there may be serious functional impairment. On clinical examination a small firm mass may be palpated. If composed principally of cartilage it may be sufficiently elastic to afford an impression of ganglion, as occurred in the case cited by Chauvain and Roux.[13]

Histologically the growths resemble benign chondroma with areas of calcification and ossification. Malignant degeneration to formation of chondrosarcoma has been observed (see below).

The treatment is excision.

MALIGNANT TUMORS

Malignant tumors of the tendons and sheaths in the hands and feet are quite rare. The clinical history is usually that of a firm swelling which may exhibit rapid or at first slow growth and which is often excised locally only to recur at the old site or in the surrounding tissues. Pain and tenderness vary both as to severity and time of onset, coming sometimes after the lesion has become well established. Because the hands and feet are so exposed to trauma, it has not been difficult to obtain clinical histories showing that the process began, at least in the patient's opinion, as the result of a single severe or of repeated traumatizations. In this group may also be placed the firm dense, often bulky, infiltrating sarcomas which arise from the plantar or palmar fascias.

Histologically, there are four types of neoplasms in this category: (1) Synovioma (Fig. 6.4). These tumors have been described in the earlier literature under a variety of names[14] because of their peculiar histologic appearance. They are generally regarded as arising from

the synovial membranes themselves and reproduce very distorted histologic pictures reminiscent of synovia. There is a groundwork of rounded or spindle cells with varying amounts of collagen. Scattered

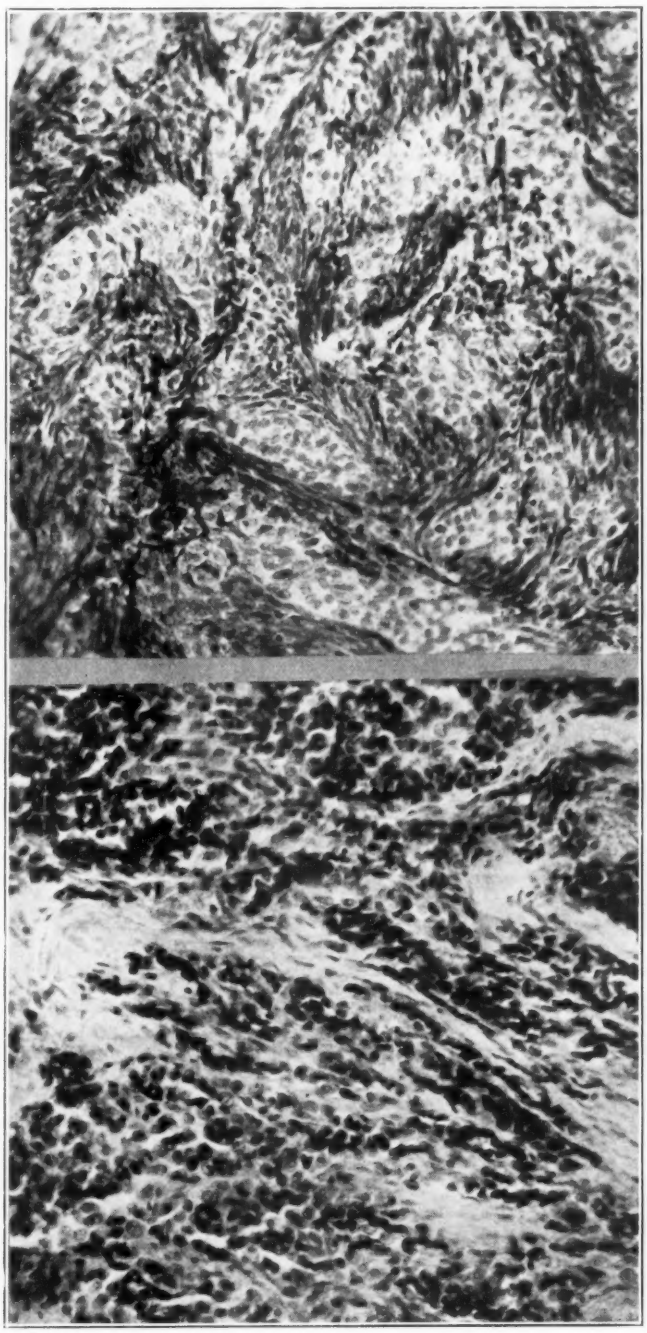

Fig. 6.—Photomicrograph (×270) of *A*, synovioma arising in tendon sheaths below internal malleolus of ankle in 36-year-old male. Note irregular cords of epithelial-like cells alternating with bundles of thin spindle cells. *B*, Round cell sarcoma of plantar fascia in 39-year-old female. Excision was followed by widespread subcutaneous metastases and death in six months.

throughout are cords or tubules of cuboidal or low columnar epithelium-like cells. In some cases small papillary cystic structures are formed where the infolded papillomatous process is not a great deal unlike a synovial villus. Mitoses in the different cells vary and their frequency in this type of tumor is no indication of malignancy. (2) So-called spindle cell sarcoma.[12] These tumors appear to be quite uncommon, arising from the tendons, sheaths, or joint capsule in the hands and feet, and indeed it may not be possible to ascertain the exact point of origin in cases that are first seen presenting a dense infiltrating mass. They may be composed of uniformly small cells, large spindle cells, or both types. The question of a neurogenic origin to such tumors has been discussed by Ewing and Stewart. (3) Round cell sarcomas (Fig. 6*B*). Tumors composed of small round cells with scanty cytoplasm and producing no stroma develop in the soft parts of the body and have been observed as primary in the hands and feet. I have had occasion to see such a patient who presented a dense egg-sized mass in the sole of the foot and who a few weeks later exhibited fulminating metastases in the subcutaneous tissues over the body and in the lungs. (4) Malignant degeneration of osteocartilaginous tendinous or synovial tumors or primary malignant chondrosarcomas of these structures have also been described.[4, 12]

General Remarks Concerning the Treatment of Malignant Tumors.— In general the treatment of choice for sarcomas well out upon an extremity is amputation at a level consistent with the principle of wide resection. In the case of the wrist or hand this should be in the midforearm, and for the ankle or foot, through the junction of the upper third with the lower two-thirds of the leg. Such treatment is indicated for primary sarcomas in the hand and foot, where the diagnosis is confirmed by biopsy and where there is no clinical evidence of axillary or inguinal lymph node or pulmonary metastases.

The question is not easily solved, however, in many of these cases where the lesion when first examined appears as a rather small, well-delimited process, and where excision, not very radical, was performed under the impression that the growth was not malignant. Microscopic study which should be done upon all such growths, when it reveals a malignant tumor, leads to a reconsideration of the future management. Where the appearance is that of a rapidly growing process, amputation should be advised. Where a synovioma is described that does not appear to be rapidly growing, and excision has been grossly wide of the lesion, postoperative x-ray therapy with frequent observation of the patient may be followed. Where it is feasible to reoperate and excise the tumor site more widely, this should be advised. The subsequent development of subcutaneous firm nodules in and about the excised tumor site should constitute an indication for amputation when biopsy of a nodule reveals its sarcomatous nature

and when roentgenograms of the chest show no evidence of pulmonary metastases.

Irradiation Therapy: Experience to date has indicated that these neoplasms are radioresistant and therefore little is to be expected from such treatment, although it is indicated where surgical procedures are refused.

Prognosis: The prognosis in general is poor, yet some cases have survived for long periods and others after surviving long periods have died of pulmonary metastases. Coley and Pierson[15] recently have published an excellent summary of the question of synovioma, reviewing the literature and the series of the Memorial Hospital.

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TUMORS PRIMARY IN THE BONES OF THE HANDS AND FEET

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IT IS ONLY very rarely that tumors of any type originate in the bones of the hands and feet. Statistics of the Memorial Hospital as well as an extensive review of the literature substantiate this statement. As has been pointed out by Kahn, malignant tumors of these bones are exceedingly rare. Schreiner and Wehr surveyed a series of 10,459 cases of malignant disease over a nineteen-year period and could find only 37 involving the foot, and only 4 of these were bone sarcomas. Of 1,740 bone tumors at Johns Hopkins Hospital, Moore found 46 benign and malignant tumors of the foot. Considering the fact that there are 206 bones in the entire skeleton, 106 of which are in the hands and feet, the disproportion in their relative frequency of involvement is apparent.

In a total of 1,211 bone tumors at Memorial Hospital and the Hospital for Ruptured and Crippled, we have found only 47 instances of involvement of the bones of the hands and feet. These are shown individually in Table I and summarized in Table II.

Sex, apparently, is an unimportant factor. In the series of 47 cases mentioned, 23 were males and 24 were females.

Regarding age, the youngest patient was 5 years of age, and the oldest, 65; the average age was 28.3 years. There were 7 cases in the first decade, 10 in the second, 12 in the third, 9 in the fourth, 4 in the fifth, 2 in the sixth, and 3 in the seventh. Thus the majority of patients (31) were between 10 and 40 years of age.

Twenty tumors involved the bones of the hand and 27 the bones of the foot. Six occupied the metacarpal bones, and 14 the phalanges of the hand (10 in the proximal, 2 in the middle, and 2 in the distal phalanges). One tumor occurred in the astragalus; 10 in the calcaneus, and 1 in the cuneiform. Ten were found in the metatarsals and 5 in the phalanges of the foot (none in the proximal, 3 in the middle, and 2 in the distal phalanges).

There were 12 cases of osteogenic sarcoma, 6 of Ewing's endothelioma, and 9 giant cell tumors. Exostoses and chondromyxomas are included under the heading of chondromas, of which there were 15. There were 2 simple cysts, 2 metastatic lesions involving the bones of the hands and feet, and 1 angiosarcoma.

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The treatment rendered and the results obtained are given in Table I, and will be discussed under the different types of tumors.

From the American and foreign literature we were able to collect a total of 609 cases of tumors involving the bones of the hands and feet. These are summarized in Table III. Some of these cases are individually reported and again included in another author's series, so that there may be some duplication. However, we have attempted to recognize this possibility and to report each case but once. Again, considerable difficulty is experienced because of inadequate details in the original report. Diagnoses are often inconclusive; the location is frequently inadequately described; scant details of the treatment are given, and in only a few instances are adequate follow-up reports available. Under these circumstances, we have endeavored to compile the statistics as given in our table as accurately as possible, with careful reference to the original report. The total number is greatly augmented by many instances (205) of subcalcaneal exostoses. There is a remarkable sparsity in the literature of all other types of primary bone tumors of the hands and feet. The proportionate number roughly corresponds to our series. The number of cases for each bone involved is shown under the various diagnoses in Table III.

Osteogenic Sarcoma.—There were 12 cases of osteogenic sarcoma in our series and 37 in the literature. The symptoms noted were those found in osteogenic sarcoma in general; i.e., pain in the region involved followed shortly after by swelling and disability. There is a hard, palpable swelling which increases in size with relative rapidity. The roentgenographs show characteristic irregular bone destruction with laying down of new bone (Fig. 1), often with a sun-burst appearance. Aspiration biopsy as recommended by Coley, Sharp, and Ellis, is a valuable aid in the accurate diagnosis of this tumor and should be done to verify the clinical and roentgenographic findings. Many of these tumors are secondary to a benign chondroma and represent a malignant transformation of a simple chondroma to an osteochondrosarcoma (Fig. 2). Not infrequently trauma is the alleged cause of this transformation. In other cases the tumors are of the fibrosarcoma variety, and these in our opinion offer a more hopeful prognosis. Five of our patients are alive and well (3 for more than five years); 4 died of pulmonary metastases from one to three years after admission; and 1 died following a prostatectomy nine years after amputation of the foot for osteogenic sarcoma. The other 2 have been lost to follow-up, but 1 is undoubtedly dead, as he had pulmonary metastases six months after treatment. From our five-year survival rate (33 per cent), it would appear that osteogenic sarcoma of the bones of the hands and feet offers a more favorable prognosis than does the same condition in other bones. It is our opinion that once a diagnosis of osteogenic sarcoma has been

TABLE I

BONE TUMORS OF THE HANDS AND FEET

SERIES FROM MEMORIAL HOSPITAL AND HOSPITAL FOR RUPTURED AND CRIPPLED

NO.	NAME	SEX	AGE	BONE*	DIAGNOSIS	ADMITTED	TREATMENT	FOLLOWED	STATUS	REMARKS
1	B. A.	F	25	L. calcaneus	Endothelioma	12/ 3/34	Curettage, x-ray, amputation	12/23/37	Well	
2	G. B.	F	8	L. phalanx, D, foot	Osteochondroma	11/ 3/37	Excision	3/23/38	Well	Pyogenic granuloma
3	J. B.	M	11	L. phalanx, D, foot	Osteochondroma	1/31/38	Excision	2/23/38	Well	
4	B. B.	M	60	L. metacarpal, v	Osteogenic	7/28/20	Excision, radium, amputation	12/ 1/29	Died	following prostatectomy
5	D. B.	F	15	L. calcaneus	Osteogenic	8/ 1/32	Amputation	12/ 9/37	Well	
6	J. B.	F	44	L. phalanx, P, hand	Chondroma	1/ 4/37	Curettage, graft	12/ 9/37	Well	
7	W. C.	F	24	L. metacarpal, v	Osteochondroma	5/27/33	Excision, three times	1/12/38	Well	
8	J. C.	F	25	R. metacarpal, i	Giant cell	11/26/34	Curettage, x-ray	12/ 2/36	Final	Not traced further
9	E. C.	F	49	L. calcaneus	Osteogenic	8/21/35	Amputation	10/26/36	Died	
10	E. C.	M	5	L. calcaneus	Giant cell	10/31/34	X-ray	5/ 6/32	Well	
11	F. C.	F	37	R. phalanx, P, hand	Chondroma	9/22/22	Radium	1/ 6/26	Final	Not traced further
12	F. C.	F	26	L. phalanx, P, hand	Osteochondroma	6/28/33	Excision	6/30/37	Well	
13	W. C.	M	30	R. phalanx, P, hand	Osteogenic	2/10/37	Amputation	6/25/38	Well	
14	D. D.	M	33	R. metatarsal	Osteogenic	8/25/29	Amputation	5/11/32	Well	
15	S. D.	M	8	R. phalanx, D, foot	Osteochondroma	3/26/30	Radium	5/14/30	Final	Not traced further
16	T. E.	M	13	L. phalanx, D, hand	Giant cell	12/12/35	Amputation	6/29/38	Well	
17	I. E.	M	30	R. phalanx, P, hand	Chondroma	9/25/36	Curettage	4/13/38	Well	
18	C. F.	M	50	R. metatarsal, iii	Endothelioma	10/17/24	Excision, radium	9/26/26	Died	Multiple metastases
19	W. F.	M	8	R. calcaneus	Osteogenic	3/18/30	Excision, radium	7/14/33	Died	Multiple metastases
20	A. G.	M	16	R. cuneiform	Osteogenic	6/12/24	Amputation	9/ 2/26	Died	Multiple metastases
21	J. G.	F	26	L. phalanx, P, hand	Osteochondroma	4/18/31	None	4/13/32	Final	Not traced
22	M. G.	F	41	R. phalanx, D, hand	Metastatic	4/22/34	Amputation	10/29/37	Died	Primary parotid

*D, distal; P, proximal.

TABLE I—CONT'D

23	S. H.	M	17	L. metacarpal, iii	Giant cell	4/28/24	X-ray	2/ 3/25	Final	Not traced
24	J. H.	M	40	R. astragalus	Metastatic	3/18/28	Radium	4/20/28	Died	Primary hypernephroma
25	E. K.	F	23	L. metatarsal, i	Endothelioma	10/25/24	Excision, radium, x-ray	4/30/25	Died	
26	G. K.	F	23	L. phalanx, P, hand	Chondroma	12/11/36	Excision	4/ 6/38	Well	
27	B. L.	M	13	L. phalanx, D, foot	Osteochondroma	12/ 1/36	Excision	4/18/38	Well	Pyogenic granuloma
28	M. M.	M	35	R. phalanx, M, hand	Osteochondroma	2/25/35	Excision	3/22/37	Well	
29	A. M.	F	53	L. calcaneus	Giant cell	9/20/34	X-ray	1/20/37	Final	Not traced further
30	H. N.	M	32	R. metatarsal, i	Giant cell	7/22/26	Curettage	11/15/37	Well	
31	S. P.	F	65	R. metacarpal, iv	Chondroma	3/18/20	Radium	5/15/23	Final	Not traced further
32	H. P.	F	8	L. phalanx, P, hand	Cyst	1/20/31	Curettage	–	–	No follow-up
33	E. R.	M	29	R. phalanx, P, hand	Chondroma	9/21/31	X-ray	11/ 9/36	Well	
34	M. R.	F	34	L. metatarsal, ii	Osteogenic	5/19/33	Amputation	5/16/35	Died	Pulmonary metastasis
35	R. S.	F	63	R. phalanx, P, hand	Chondroma	12/14/35	None	–	–	No follow-up
36	P. S.	M	19	R. metacarpal, i	Osteogenic	9/ 3/24	Excision, radium, x-ray	6/ 9/27	Final	Pulmonary metastasis 1/30/25
37	T. S.	M	27	L. calcaneus	Endothelioma	4/ 2/22	X-ray	6/30/24	Final	Not traced further
38	J. S.	M	65	R. metatarsal, v	Osteogenic	5/ 8/31	X-ray, amputation	11/17/37	Well	
39	R. S.	F	16	R. phalanx, D, foot	Osteochondroma	6/ 6/34	Excision	7/21/37	Well	Pyogenic granuloma
40	C. S.	F	5	L. calcaneus	Endothelioma	12/ 1/23	Radium	2/15/27	Died	Multiple metastases
41	H. S.	F	17	L. metatarsal, iv	Giant cell	8/30/37	Curettage (recurred), excision	4/13/38	Well	
42	M. S.	F	14	L. calcaneus	Giant cell	10/ 2/29	Curettage, x-ray, amputation	4/19/37	Well	
43	B. T.	F	32	R. phalanx, D, hand	Cyst	8/16/29	Curettage	–	–	No follow-up
44	C. T.	M	9	L. calcaneus	Endothelioma	10/ 3/23	Curettage, radium	4/14/24	Died	Multiple metastases
45	V. V.	M	23	R. metatarsal, i	Osteogenic	7/23/24	Excision, x-ray	1/ 7/28	Final	Not traced further
46	R. V.	M	33	R. metatarsal, iii	Angiosarcoma	4/26/25	Amputation	5/ 5/25	Died	Multiple metastases
47	L. W.	F	34	R. metatarsal, iv	Osteogenic	3/ 3/30	X-ray, radium, curettage, amputation	2/14/38	Well	

TABLE II

SUMMARY OF MEMORIAL HOSPITAL AND HOSPITAL FOR RUPTURED AND CRIPPLED CASES

	OSTEOGENIC SARCOMA	EWING'S ENDOTHELIOMA	GIANT CELL TUMOR	CHONDROMA	CYST	METASTATIC	ANGIOSARCOMA	TOTAL
Metacarpals	2		2	2				6
Phalanges 1	1		1	7	1			10
Phalanges 2			1	1				2
Phalanges 3					1	1		2
Astragalus						1		1
Calcaneus	3	4	3					10
Tarsals	1							1
Metatarsals	5	2	2				1	10
Phalanges 1								
Phalanges 2				3				3
Phalanges 3				2				2
Total	12	6	9	15	2	2	1	47

made the treatment of choice is primary amputation. Local excisions and resections, with or without irradiation, have been tried by others, but we know of no five-year cure following these procedures. Of course, partial amputations of the hand and foot may be justified according to the extent and location of the lesion (Fig. 3). Thus, it may be possible to preserve a portion of the member and leave the patient with a functionally useful remnant, an impossible accomplishment when dealing with tumors of other parts of the skeleton.

Endothelioma (Ewing's Sarcoma).—We have 6 cases of this condition in our series, and there are 31 in the literature. The onset is often indefinite and a diagnosis of chronic osteomyelitis frequently is erroneously made. Again, pain is the earliest symptom and there is often fever. The roentgenograph shows bone destruction of a more

TABLE III

SUMMARY OF CASES COLLECTED FROM THE LITERATURE

UPPER	OSTEOGENIC	ENDOTHELIOMA	GIANT CELL TUMOR	CHONDROMA	MYXOMA	CYST	METASTATIC	EXOSTOSIS	OSTEOID OSTEOMA	SARCOMA	TOTAL
Carpals		1				1		4			6
Metacarpals	2		11	7	1	7			1		29
Phalanges	2	1	9	54	7	16		12			101
Total (hand)	4	2	20	61	8	24		16	1		136
LOWER											
Astragalus	3		10	1	1	3			1		19
Calcaneus	21	21	17	4	1	7	1	205	1	1	279
Tarsal (other)	4		5	2		2	2	3		1	19
Metatarsal	3	6	9	7		5	2	3		3	38
Phalanges	2	2	4	16	1	6	2	84	1		118
Total (foot)	33	29	45	30	3	23	7	295	3	5	473
Total	37	31	65	91	11	47	7	311	4	5	609

Fig. 1.—Case 5. Osteogenic sarcoma of the os calcis. Female, aged 15 years. Amputation below the knee. Alive and well 5½ years later.

Fig. 2.—Case 38. Osteogenic chondromyxosarcoma of fifth metatarsal. Male, aged 65 years. Diagnosis by aspiration biopsy. Amputation of fourth and fifth metatarsals. Alive and well 7½ years later.

or less diffuse nature, but the fusiform shape and the periosteal splitting (features characteristic of this disease in the long tubular bones) are less frequently demonstrable. In this type of tumor, also, aspiration biopsy is relatively simple and accurate and should be attempted if there is any doubt as to the diagnosis of a destructive bone lesion. The condition is frequently referred to in the older literature as round cell sarcoma, later as endothelial myeloma, and currently as endothelioma or Ewing's sarcoma. Probably some hemangioendotheliomas

Fig. 3.—Case 13. Low grade osteogenic sarcoma of proximal phalanx of fifth finger. Male, aged 30 years. Two operations elsewhere for inflammatory disease. Amputation of fourth and fifth fingers through metacarpals. Alive and well 1½ years later.

and unclassified sarcomas belong in this group. One of our cases was diagnosed following curettage for osteomyelitis of the os calcis; heavy irradiation was given, followed by amputation and a prolonged course of Coley's toxins; the patient is well more than three years after with no evidence of metastasis or recurrence. Four other patients (2 os calcis and 2 metatarsal bone) died of multiple metastases from nine months to three and one-half years after treatment. One case

was lost to follow-up after two years. It is, therefore, fair to assume that the prognosis of this condition is generally poor. However, it is our impression that the treatment of choice, following early diagnosis, is heavy irradiation followed by amputation and a postoperative course of injections of Coley's toxins. Connor reports a patient of Thompson's in the Bone Sarcoma Registry who died following a gall-bladder operation eight years after amputation of the foot for endothelioma of the os calcis.

Fig. 4.—Case 16. Aneurysmal giant cell tumor of distal phalanx of thumb. Male, aged 13 years. Amputation through proximal phalanx. Well two years.

Giant Cell Tumor.—In addition to 9 giant cell tumors in our own series, we found 65 reported in the literature. Vague pain is usually an early symptom. Not infrequently, however, slight swelling or pathologic fracture is the first symptom, as these tumors are benign and grow relatively slowly. They may attain considerable size before the patient seeks medical relief (this was true of one case in our series [Fig. 4]). The roentgenographic appearance is usually quite characteristic and shows a round or oval centrally placed lesion with many fine trabeculations, usually well demarcated and with a thinned but intact cortex (Fig. 5). The clinical and roentgenographic features are usually sufficient to make a diagnosis. Aspiration biopsy may be tried if the cortex

is very thin, but it is not as useful in this type of tumor, as they are usually centrally placed. The terms hemorrhagic osteomyelitis and myeloid sarcoma appearing in the literature are synonymous. In the microscopic picture numerous giant cells are characteristic, but the aggressiveness of the tumor depends upon the fibrous tissue stroma which must be given due consideration in the ultimate pathologic diagnosis.

Following a recent extensive survey of giant cell tumors in general,* we have come to the conclusion that the treatment of this con-

Fig. 5.—Case 41. Giant cell tumor of fourth metatarsal. Female, aged 17 years. Curettage at another hospital. Recurred six months later. Resection of metatarsal. Well four months later.

dition is either surgery or irradiation, but never both. Either procedure alone gives satisfactory results; whereas, a combination is fraught with danger. We believe the same principle applies to giant cell tumors of the hands and feet. Irradiation, if used, should be given in moderate doses. Radical surgery, such as amputation or resection, is indicated only in special instances. One of our cases presented a tremendous growth of the distal phalanx of the thumb, and amputation was performed as the treatment of choice (Fig. 4). Astragalectomy and resection of the tarsals, metatarsals (Fig. 5), or metacarpals may

*Coley, Bradley L., and Higinbotham, Norman L.: Giant Cell Tumor of Bone, J. Bone & Joint Dis. **20**: 870-884, 1938.

be necessary in recurrent cases. However, curettage, cauterization with zinc chloride, and primary wound closure is indicated in most cases as the primary treatment.*

Cyst.—Our series contains 2 cases of simple cyst, or solitary osteitis fibrosa cystica; whereas, there are 47 cases reported in the literature. In many of the reported cases, however, the diagnosis was based on clinical and roentgenographic evidence alone, but, were a study of the pathologic material possible, we feel sure that not a few would be transferred to the giant cell tumor or chondroma group. These cysts give very few signs and symptoms and are usually picked up as an incidental finding in roentgenographs taken for other purposes. Pathologic fracture is frequently the first symptom. The roentgenograph shows a small rounded area of bone destruction with well-defined margins, but lacking the trabeculations characteristic of giant cell tumors. Operation usually reveals a thin, fibrous lining of the cyst wall, containing clear yellowish fluid.

Surgery has always been the method of choice and results are usually excellent with simple curettage after unroofing the cavity. In the larger cysts, or after pathologic fracture has occurred, slivers of bone may be implanted within the cavity.

X-ray therapy may be used and with satisfactory end results. However, a degree of uncertainty is inescapable and results are obtained much more slowly than after surgical treatment. Moreover, the hands and feet are to be regarded as regions where the late effects of irradiation may prove serious, and obliterating endarteritis is a particular hazard in these localities. For these reasons, surgery is generally to be preferred.

Chondroma.—Our series includes 15 chondromas (4 subungual exostoses); in addition there were 91 reported in the literature. These tumors consist largely of cartilage. Their common designation is central chondroma or osteochondroma, according to the direction of their growth; i.e., central or outward. Preferable and more descriptive are the terms enchondroma and ecchondroma. In the opinion of Gatewood, enchondromas arise from pre-existing cartilage and are probably congenital, due to an abnormal anlage in the intermediate cartilage of the bone involved. Some pathologists believe that they spring from islands of cartilage left in abnormal situations and hence may grow from the marrow in the phalanges, metacarpals, etc. Ecchondromas occur independently of any cartilaginous anlage and present themselves as an overgrowth arising where cartilage is normally present.

The central variety presents symptoms similar to those of a simple cyst or giant cell tumor, pathologic fracture being a common first symptom. While the roentgenographic appearance also presents features of

*Coley, Bradley L., and Higinbotham, Norman L.: Surgical Treatment of Giant Cell Tumor, Ann. Surg. **103**: 821, 1936.

both, as a rule they appear more multiloculated. The trabeculations are coarser and usually the entire shaft of the bone is involved. Irradiation therapy has been tried with success in a number of cases, but as they are particularly radioresistant prolonged treatment is required. One case in our series did not present roentgenographic evidence of healing until four and one-half years after the first treatment. Operation is preferable and is similar to the conservative operation for giant cell tumor; namely, thorough curettage, cauterization with zinc chloride, and primary wound closure (Fig. 6). It is important to remove all traces of tumor tissue, as this type of tumor is prone to recur if not

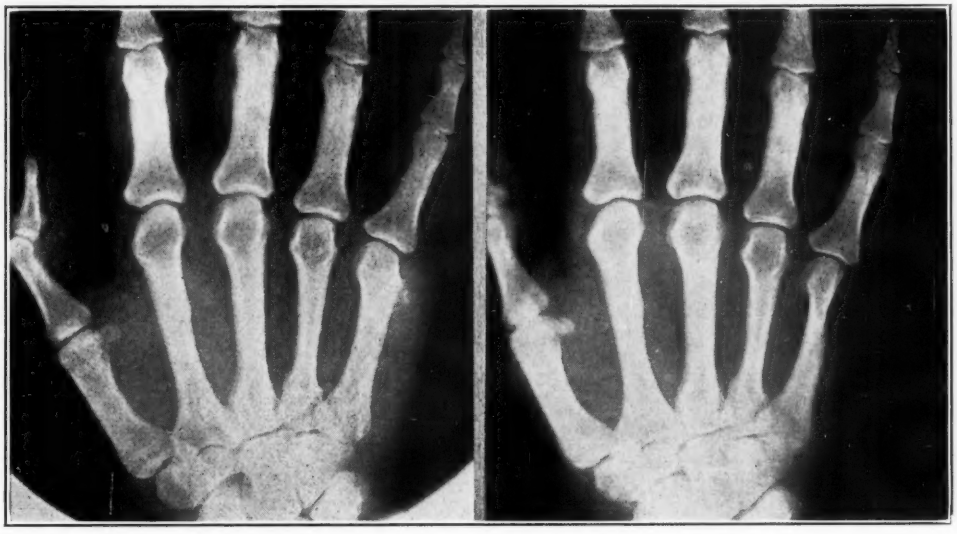
Fig. 6.—Case 17. Central chondroma of proximal phalanx of fourth finger. Male, aged 30 years. Curettage, cauterization and primary wound closure. No recurrence after two years.

adequately removed. As in cysts, small tibial bone grafts may be advisable when there has been much destruction or when pathologic fracture has occurred. We obtained an excellent result in the proximal phalanx of the ring finger with this latter procedure.

Ecchondromas are more apt to produce symptoms of pressure, due to their bony outgrowth, and frequently their first symptom is the detection of a bony protuberance. They are seen in the roentgenographs as definite bony outgrowths, usually with a broad base. Irradiation therapy has been tried, but it effects little, if any, regression in the

size of the tumor, due to its radioresistance. If they are causing symptoms, they should be removed by operation, care being taken to remove with the chisel a generous wedge-shaped portion at the base. Again complete removal is essential, as they are prone to recur if inadequately excised. One case in our series recurred twice and a third operation was necessary for complete relief (Fig. 7). Four other cases in our series showed excellent results following wide local excision.

Undoubtedly subungual exostosis should be grouped with the latter condition. We had 4 cases, all occurring as pyogenic granulomas of the great toe (Fig. 8). Our cases are grouped under the diagnosis of chondroma in Table II; whereas, the larger number occurring in the



A. *B.*

Fig. 7.—Case 7. *A*, Osteochondroma (ecchondroma) of the fifth metacarpal. Female, aged 24 years. Excision. Recurred eight months later. Second excision. Recurred two years later. Third excision. *B*, Result 1½ years after third operation.

literature appears under the diagnosis of exostosis in Table III. According to Davidson, the patient first notices that the nail is being slowly raised from the usual flat position, and then there appears a hard growth from beneath the nail which pushes the nail backwards. The growth increases gradually in size until the nail becomes almost vertical in its axis. Mason states that the condition is most common in the foot (usually in the great toe) and that there are only a dozen cases reported as occurring in the hand (usually in the index finger). The roentgenographs generally show a characteristic bony outgrowth, but occasionally they may be negative if ossification has not occurred (Kurtz). Mason recommends removal with the least possible damage to the nail bed. Some authors recommend removal of the nail and removal of the growth with chisel and gouge, cauterizing the base

with phenol. Lapidus describes a more radical operation, employing a U-shaped incision, resecting the nail, and then resecting the distal half of the distal phalanx. He uses a long posterior and a short anterior flap. Any of these procedures may be employed, depending upon the size of the growth and the conditions present in the individual case.

Fig. 8.—Case 39. Subungual exostosis of big toe. Female, aged 16 years. Resection of distal half of nail, excision of exostosis, and base cauterized with zinc chloride. Pinch grafts to denuded area. Excellent result. No recurrence three years later.

Myxoma.—While our series contains no example of pure myxoma, 11 were found reported in the literature. The symptoms, signs, and roentgenographic appearance closely resemble those of chondromas and cysts. The differential diagnosis is extremely difficult and usually can be made on histologic examination alone. The operative or preoperative diagnosis is extremely important, however, because, as Kahn points out, these tumors require special treatment and are the most transplantable of all tumors. Thorough curettage must be employed and cauterization

is essential, as these tumors are extremely prone to recur. In this event Bloodgood recommends amputation.

Not infrequently chondromatous and myxomatous elements are mixed in the one tumor, producing a chondromyxoma. Some of these have been included under chondromas and others under myxomas in Table III, depending upon the author's description. The more the myxomatous element predominates, the more requisite it is to treat them as pure myxomas.

One must always bear in mind the grave possibility that a chondroma, myxoma, or chondromyxoma may undergo malignant transformation. It is for this reason that, however minor the symptoms, we believe with Campbell that they should be removed by operation at the earliest possible moment.

Calcaneal Spurs.—No examples of this condition have come to our attention in the Bone Tumor Clinic, as they are a not uncommon orthopedic problem dealt with by orthopedic surgeons. There are 205 cases reported in the literature. They are more common in the male and are often bilateral. The symptoms are usually acute and begin with pain in the heel, sometimes accompanied by swelling, so that the patient walks on his toes and forefoot with a characteristic gait. The acute attack may subside, but it is prone to recur, each subsequent attack being more prolonged. There is definite tenderness over the tubercle of the os calcis and roentgenographs show a characteristic exostosis. Formerly this condition was always attributed to gonorrhea, but actually this infection probably accounts for very few cases. It has been amply demonstrated that calcaneal spurs may be due to trauma, subacute gout, rheumatism, excessive standing, tuberculosis, or syphilitic epiphysitis (Warrack). Probably those due to gonorrhea and other infections occur as a local periostitis in which new bone is laid down and with each exacerbation additional layers of bone are deposited, the final result being a nodular mass of bone known as a spur (Lloyd).

Meisenback believes that spurs are actually bone formation and not a periostitis. Openshaw describes them as an overgrowth of the tubercle on the under surface of the os calcis, where the abductor minimi digitorum and the flexor brevis digitorum muscles attach. The treatment consists of general and local measures. The primary focus of infection must be sought for and dealt with. Meanwhile, a cushioned heel should be tried in the shoe. If the painful heel continues, operation for removal of the spur is indicated, and about 30 per cent of the cases will require operation. Simple excision with a chisel is usually sufficient. In more advanced cases larger incisions are required to expose the tubercle more adequately and, after removing the spur with a chisel, the base is curetted and touched with carbolic acid. Steindler's operation is indicated in recurrent cases. Lloyd stresses the importance of always excising the bursa that forms, and Chang describes a modified operation

in which a fascial transplant is placed over the denuded area after excision of the spur. Postoperative roentgenographs should be taken in order to be sure of complete removal of the spur.

Liberson employed deep x-ray therapy with gratifying results in 31 cases of painful heel, all of the gonorrheal type. This method of treatment merits a more extensive trial.

Osteoid Osteoma.—In 1932 Jaffe and Mayer described an osteoblastic osteoid tissue-forming tumor of the fourth metacarpal in a 15-year-old girl, and in 1934 Jaffe described 5 additional cases of a similar nature, 3 of which involved the bones of the hands and feet. They state that this tumor presents some features common to osteogenic sarcoma, but that it shows a benign behavior. It is well encapsulated, but capable of malignant transformation. It is usually diagnosed as inflammatory, but no pus is found at operation. On microscopic examination there are no features to suggest an inflammatory origin. All their cases were operated upon, the cavities cleaned out, and all had good results.

Unclassified Sarcoma.—There are 5 cases described in the literature as sarcoma without further differentiation as to type. Three were in the metatarsals, 1 in the cuneiform, and 1 in the os calcis. We had 1 patient with an angiosarcoma of the metatarsal who died of multiple metastases one year after amputation of the foot.

Metastatic Carcinoma.—There are 2 cases of metastatic carcinoma in our series; 1 in the phalanx of a finger from a parotid tumor, and 1 in the astragalus from a hypernephroma. In addition we saw a metastasis to the phalanx of a finger from a breast carcinoma. There are 7 instances in the literature of metastatic involvement of the bones of the foot.

General Diseases.—The bones of the hands and feet may be involved in some of the generalized bone diseases. Thus, in von Recklinghausen's osteitis fibrosa cystica (hyperparathyroidism) these bones may show manifestations of the generalized decalcification and cystic formation. Achondrodysplasia with multiple cartilaginous exostoses also may involve the bones of the hands and feet. In osteopetrosis (marble bones, Albers-Schönberg disease) one of the characteristic features early in the disease is the dense, banded appearance of the phalanges, metacarpals, and metatarsals. Paget's osteitis deformans also may extend to these bones, and it is conceivable that melorheostosis also may progress to below the wrist and ankle. The extensive involvement of multiple or plasma cell myeloma also may include the bones of the hands and feet.

SUMMARY

In a series of 1,211 tumors of bone observed at the Memorial Hospital and the Hospital for Ruptured and Crippled, only 47 were found to involve the bones of the hands and feet. The entire literature contains

only 609 cases, one-third of which were subcalcaneal spurs. While the symptoms and signs are similar to those of tumors in other parts of the skeleton, the roentgenograph reveals dissimilar pathognomonic features. Aspiration biopsy is an important diagnostic aid. The treatment is essentially the same as that indicated for tumors of other bones. The ultimate prognosis, on the whole, would seem to be more encouraging. Finally, we would reiterate the dictum that persistent pain in the bones of the hands and feet, as in any bone, is an important first symptom and should be regarded with deep suspicion as indicating the possible existence of a primary bone tumor.

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Editorial

Heparin and Thrombosis

ATTENTION was first called to heparin in 1916 by Jay McLean, now a surgeon, who was at that time a medical student working in the laboratory of Professor W. H. Howell. This anticoagulant was obtained from the liver and was named heparin. Howell and his collaborators subsequently studied the distribution and chemical properties of heparin and succeeded in purifying it further. They pointed out its possible uses in clinical medicine. However, it was still considered unsafe for use in patients.

Professor Charles H. Best, of Toronto, became interested in heparin in 1929 and he visualized clearly its possible use in clinical as well as in physiologic work. With this in view, Charles and Scott began an attempt to obtain a highly purified preparation. They succeeded finally in obtaining from lung a crystalline barium salt of uniform potency. This was one hundred times as potent as the original crude material and was completely free of toxic properties. Charles found that the barium can be completely removed, that the heparin can be stored as a dry powder, and that a solution which can be sterilized by filtration can be made from this powder.

After having obtained a highly purified form of heparin, the physiologists and surgeons of the Toronto group began their studies on animals and patients. The results illustrate once again the value of animal experimentation in the advancement of clinical medicine and the great advantage of cooperative research when a problem needs to be attacked from various viewpoints. It was observed that heparin is effective when administered subcutaneously as well as when introduced intravenously. The best procedure in its administration was thought to be to give a small dose intravenously and to follow this with a constant intravenous injection. The clotting time of the blood in this way could be set at a chosen level and maintained there for long periods. In both experimental and clinical work, approximately 40 units of heparin per kilogram of body weight were given intravenously and this was followed with a continuous injection of approximately 30 units per kilogram an hour. The clotting time was usually maintained at from twenty to thirty minutes.

Many significant experiments were performed on animals, only a few of which will be mentioned. The effects upon the mixed thrombus, which is formed when veins are injured by mechanical or chemical means, were studied. The thrombus formation which was associated usually

with a given injury did not occur when the insult was followed by the administration of heparin for seventy-two hours. Other experiments showed this to be true in the coronary arteries of the heart as well as in the peripheral veins. The white thrombus is the nucleus from which the mixed thrombus grows, and for this reason the Toronto group determined the effect of heparin on the formation of white thrombi. By allowing blood to flow over glass and cellophane tubing, it was found that heparin prevented the formation of thrombi which usually appear under these circumstances. Dr. D. W. G. Murray found that the percentage of successful end-to-end blood vessel anastomoses was considerably higher in the instances in which heparin was used. There is no doubt that nontoxic heparin will be a most valuable addition to the study of many problems in the laboratory, such as the anastomoses of blood vessels, transplantation of organs, exchange transfusions, and determinations of the rate of blood flow.

It is uncertain whether heparin is a normal constituent of the blood and whether it is the normal anticoagulant. Its wide distribution in the body suggests that it serves a physiologic function. There is excellent evidence that heparin is responsible for the markedly prolonged coagulation time of the blood in anaphylactic and peptone shock. Waters, Markowitz, and Jaques obtained from the blood of the shocked animal much more heparin than can be detected in the blood of the normal animal while the heparin content of the liver in shock was decreased.

Following the obtaining of highly purified preparations of heparin, clinical investigations were begun by Dr. Murray and associates in Toronto and by a number of workers in Sweden. Most of their efforts thus far have been centered upon attempts to prevent postoperative thrombosis and embolism. The importance of this condition is illustrated by the fact that approximately 6 per cent of the deaths following operations are due to massive pulmonary embolism and probably a larger percentage of the instances of pneumonia and lung abscesses may be due to smaller emboli. It is difficult to assess the value of heparin or any other therapeutic means as a preventive of postoperative thrombosis, but it may be said that the results thus far are encouraging and there have been no untoward experiences. It has been used by Murray without a fatality in a fairly large number of patients in the after-treatment of prostatectomy, splenectomy and other operations in which thrombosis and embolism are common. The intravenous administration of heparin is begun two or more hours following the operation and is continued for at least several days. It should be stated, however, that good results have been obtained by Bancroft and others by the use of a prophylactic regimen including the intravenous injection of sodium thiosulfate, large quantities of fluid by mouth, and the restriction of fats and carbohydrates in the diet.

As new findings are unearthed, it seems likely that heparin may be indicated in a variety of clinical conditions and operations. Among these may be included blood vessel anastomoses, peripheral embolism and embolectomy, phlebitis, coronary thrombosis, cerebrovascular thrombosis, and blood transfusions. Heparin may be used in the latter procedure either by adding it to the blood as it is collected or by injecting it into the donor. In the anastomoses of blood vessels, regional as well as general heparinization may be used. If the problem of the homotransplantation of organs is ever solved, it is probably there that heparin will find its greatest field of usefulness. Deterrents to the more general use of heparin at the present time include the discomfort to the patient of continuous intravenous injection, the increased nursing care and the price of the heparin. It costs about $80.00 per patient if the blood of an adult is to be rendered incoagulable for several days. However, if time and additional work substantiate the findings referred to already, it is likely that most of these objections can be overcome. If the demand for heparin increases, the laboratories probably will be able to reduce the price. Furthermore, some bright worker probably will synthesize this substance. In the meantime, it should be determined whether or not heparin interferes with the healing of incisions and with the normal responses of the body to infection. Furthermore, the contraindications, if any, to its use should be established.

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Recent Advances in Surgery

Conducted by Alfred Blalock, M.D.

BEZOARS AND CONCRETIONS

A Comprehensive Review of the Literature With an Analysis of 303 Collected Cases and a Presentation of 8 Additional Cases

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(Continued from the December issue.)

Diagnosis.—The diagnosis of bezoars is not difficult if the condition is borne in mind. The relative rarity of these cases is conducive to the usual inadvertency or negligent inconsideration of the attending physician for the possible presence of these intragastric foreign bodies, thus forming the basic difficulty in their diagnosis. If for no other reason than as a reminder, their occasional presentation is thoroughly justified. Once the condition is suspected, the establishment of a correct diagnosis should be relatively simple.

In considering the diagnostic basis of trichobezoars, it should be recalled that a careful interrogation into the patient's previous habits in early childhood or adolescence frequently will educe the suggestive clue of trichophagia. Whereas the patient usually denies this hair-eating custom, it can usually be obtained from the parents or relatives. This was possible in over one-half of the collected cases (Graph VI). The great majority of these patients are girls or young women. This is demonstrated clearly by the series of collected cases, in which over 90 per cent were females and over 80 per cent were under the age of 30 years (Graphs III and IV). The presence of characteristic clinical manifestations, such as a rather large, firm, freely movable epigastric mass accompanied by some pain, nausea and vomiting, and anorexia, weakness, and loss of weight, is corroborative evidence. In the collected cases these symptoms and signs were prominently present. Fever is conspicuously absent. The presence of long strands of hair in the stools or in the gastric contents is confirmatory evidence. Usually there is a slight secondary anemia with a mild leucocytosis. Such a clinical picture, together with the characteristic fluoroscopic and roentgenologic findings previously described, will justify a diagnosis of trichobezoar. Whereas formerly in the absence of systematic roentgenologic examinations the diagnosis was usually made during the exploratory operation, at present, with the almost ubiquitous use of roentgenography, the lack of a correct preoperative diagnosis is indicative of misfeasance on the part of the physician.

The diagnosis of diospyrobezoars and other phytobezoars is also not attended with considerable difficulty if the condition is kept in mind. Again a careful inquiry into the patient's previous eating habits will often elicit the possibility. Thus, over 80 per cent of the collected cases of diospyrobezoars including the authors' gave a history of persimmon ingestion (Graph VI). In contrast to trichobezoars, approximately 80 per cent of the patients with phytobezoars are of the male sex and over 30 years of age (Graphs III and IV). Characteristically the clinical manifestations consist of a freely movable, firm abdominal mass usually located in the epigastrium and readily displaced beneath the left costal margin, associated with some pain or tenderness, nausea and vomiting, and moderate weakness or loss of weight. Constipation or diarrhea occurs in about one-third of the cases. Fever is prominently absent. If in addition to these findings there is a very slight secondary anemia and a mild leucocytosis, one should be even more suspicious of a phytobezoar. Gastric analysis reveals little more than probably a slight hyperacidity and stool examinations are not significant. However, in the presence of such a clinical picture the characteristic fluoroscopic and roentgenographic appearances previously described should definitely establish the diagnosis.

As an added diagnostic procedure, Moersch and Walters[223] recently have advocated direct visualization by means of gastroscopy. Whereas this undoubtedly is a valuable diagnostic aid, at present its usefulness is limited because there is required necessarily a special instrument and a high degree of skill.

The possibility of such complications as intestinal obstruction and gastroduodenal ulceration with consequent hemorrhage, perforation, and peritonitis always should be borne in mind. Obviously these complications assume different but characteristic clinical manifestations and therefore render the diagnosis of the original condition more perplexing. However, in the presence of such an eventuality the diagnosis of the complication is certainly more important.

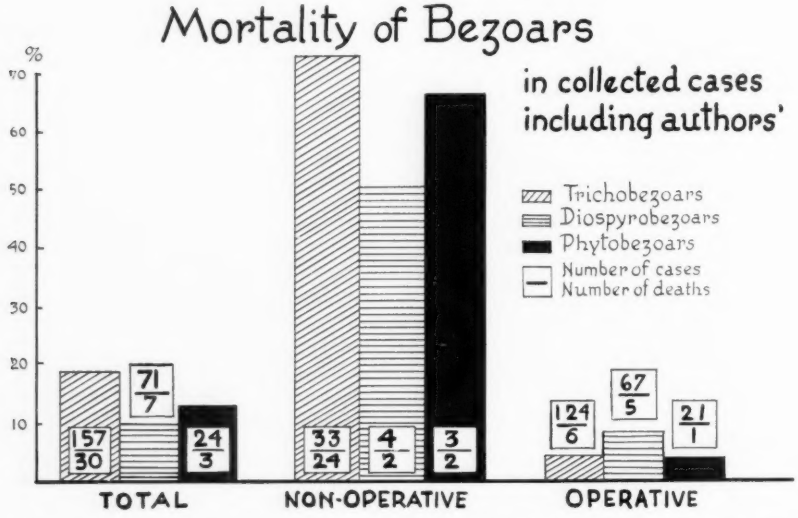
Prognosis.—The prognosis in bezoars depends primarily upon the presence or absence of two factors: (1) the institution of adequate therapy, and (2) complications.

That the institution of proper therapy is an important factor in the prognosis is readily evinced by the fact that the mortality in the nonoperative collected cases of trichobezoars, diospyrobezoars, and other phytobezoars is 72.7 per cent, 50 per cent, and 66.6 per cent respectively, in contrast to the corresponding incidences in the operative cases of 4.8 per cent, 7.4 per cent, and 4.7 per cent (Graph VII). The significance of complications in the prognosis is clearly demonstrated by the fact that, whereas the mortality in the collected cases of trichobezoars and phytobezoars with complications is 53.1 per cent and 18.7 per cent respectively, in those cases without complications these corresponding

figures are 10.4 per cent and 2.1 per cent (Graph VIII). The total mortality in the collected cases of trichobezoars, diospyrobezoars, and phytobezoars, including ours, was 19.1 per cent, 9.8 per cent, and 12.5 per cent respectively (Graph VII).

Curiously enough the operative mortality in trichobezoars has not been diminished during the past three decades since Matas' publication. Whereas, in 1914, according to Matas, there were 2 deaths (4.1 per cent) in 48 cases operated upon, at present of 124 cases operated upon 6 (4.8 per cent) died.

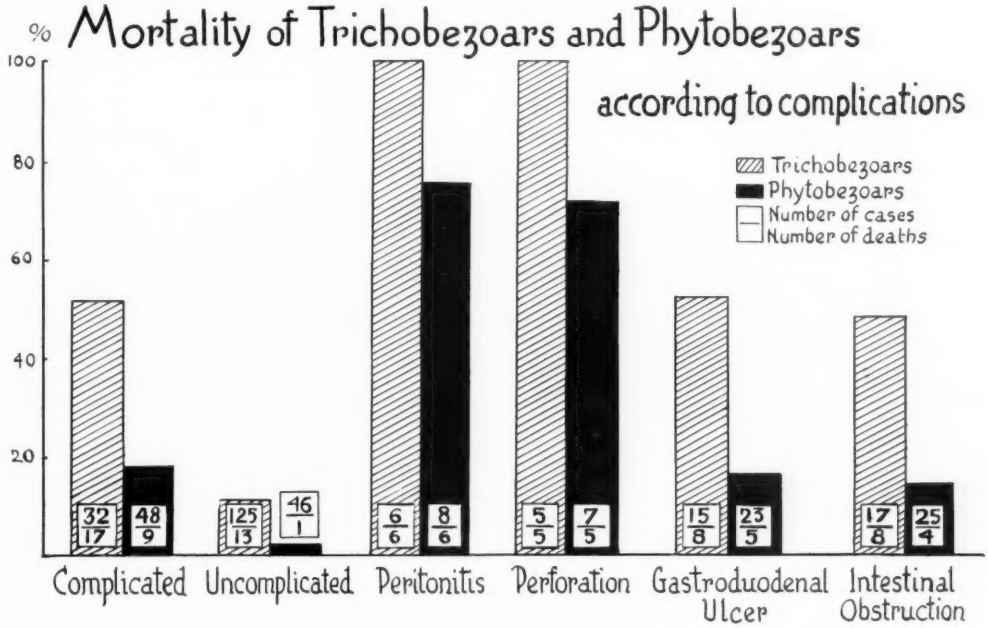
An analysis of the cause of death in the collected cases of bezoars is significant. It will be observed from Graph IX that intestinal obstruction occurred in 17 (10.8 per cent) of 156 collected cases of trichobezoars and 25 (26.5 per cent) of 94 collected cases of phytobezoars



Graph VII.—Comparative mortality rates based upon 252 collected cases of bezoars, including those of DeBakey and Ochsner.

including ours. Whereas of the 17 cases of trichobezoars, 8 (47 per cent) died; of the 25 cases of phytobezoars only 4 (16 per cent) died. This considerable difference in mortality rates in the two types of bezoars is probably due to the fact that the patient with trichobezoar is usually in a weaker and more exhausted condition by virtue of a longer duration of the original, larger intragastric foreign body. In our series of 7 cases of phytobezoar, there were 3 (Cases 4, 5, 6) with intestinal obstruction. Two of these (Cases 5 and 6) were treated conservatively and 1 (Case 6) eventually passed the bezoar in the stool; whereas the other (Case 5), admitted in extremis, died within twenty-four hours. The third patient (Case 4) was operated upon on a service other than ours and the bezoar was removed through an enterostomy. The patient's progress was very satisfactory for four days postoperatively under a physiologically rational postoperative therapy. However, on the fourth postoperative

day this was discontinued and ice water, fruit juices, and sweetened soda water drinks were administered. The following day the temperature rose to 103° F., the pulse became rapid, there was marked abdominal distention, and the patient vomited everything administered. Enemas were given with no apparent relief in the distention. Under this regimen for four days the patient became progressively worse, then the heat tent and Wangensteen suction were applied, but by this time the patient was beyond even heroic measures and died the following day. Whereas it would be inopportune to attempt here a detailed discussion of metalaparotomy therapy based on physiologic principles, it is worthy of emphasis because this case illustrates in such a tragic but strikingly significant manner the fallacious and even disastrous irrationality of



Graph VIII.—Graphic representation of mortality in collected cases of bezoars according to complications.

the postoperative administration of ice water, fruit juices, and sweetened soda water beverages. This has been discussed adequately in previous publications.[330-332] It is our firm conviction that even upon the day following the development of marked abdominal distention, hyperpyrexia, and vomiting, had the administration of iced and sweetened beverages been discontinued and the patient again placed on the more rational postoperative therapy consisting of (1) Wangensteen suction, (2) pleboclysis of glucose and saline, (3) heat tent over the abdomen, and (4) morphine, the outcome probably would have been different.

Fifteen (9.6 per cent) of the collected cases of trichobezoars and 23 (24.4 per cent) of the collected cases of phytobezoars were complicated by gastroduodenal ulceration (Graph IX). Whereas of the 15 cases

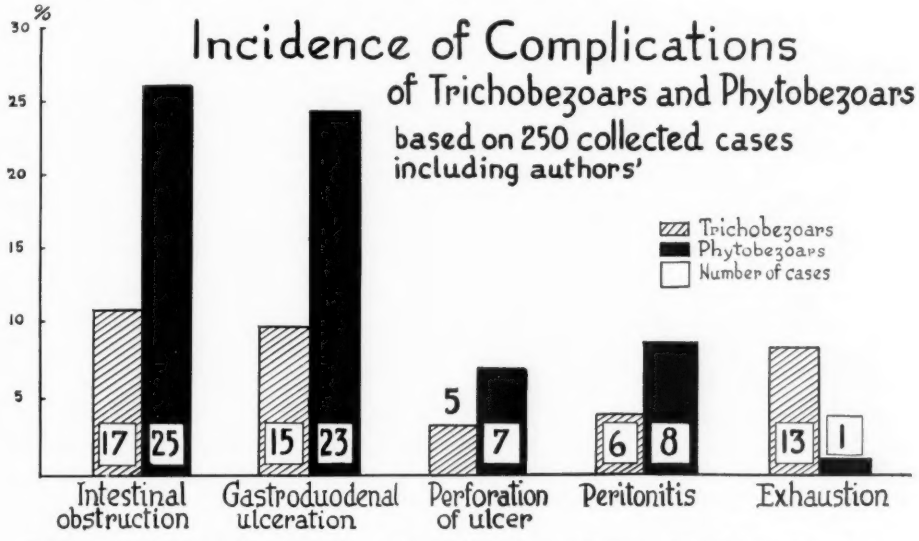
of trichobezoars with ulcers, 8 (53.3 per cent) died; of the 23 cases of phytobezoars only 5 (21.7 per cent) died (Graph VIII). These contrasting mortality rates in the two types of bezoars are due probably in great measure to the difference in the intragastric contents. The foul, putrid material characteristically associated with trichobezoars undoubtedly contains more virulent pathogenic organisms than the relatively sterile intragastric contents of phytobezoars. This is further corroborated by the fact that all of the 5 cases of trichobezoar ulcers that perforated died; whereas, of the 7 cases of phytobezoars with perforated ulcers only 5 (71.4 per cent) died (Graph VIII). In this regard the fact that all of 6 cases of trichobezoars that developed peritonitis died and only 6 of the 8 cases of phytobezoars with peritonitis died is significant (Graph VIII).

The *complications* resulting from the various types of bezoars are due primarily to: (1) interference with the normal physiologic activity of the gastrointestinal tract, namely, obstruction and exhaustion or inanition; and (2) traumatic irritation to the stomach and bowel wall and its consequences, mucosal erosion, ulceration, perforation, and peritonitis. The occurrence of such complications is readily comprehensible upon the realization that bezoars, in the final analysis, are simply foreign bodies in the gastrointestinal tract. Obviously, the complication produced depends essentially upon the primary mechanical effect of the foreign body upon the normal physiology of the stomach and intestines. Thus, a trichobezoar may gradually grow to such enormous proportions that the stomach can no longer compensate for its presence and additional space required by food ingested. The arrival of this degree of tolerance is then manifested usually by vomiting and the patient actually starves to death of inanition and exhaustion unless appropriate therapy is instituted. In a series of 156 collected cases of trichobezoars this eventuality occurred in 13, an incidence of 8.3 per cent. On the other hand, this complication occurred in only 1 of 94 collected cases of phytobezoar (Graph IX). This difference may be accounted for by the fact that the latter type of bezoar is more likely to be of smaller dimensions and less likely to increase in size.

Another mechanical effect of bezoars is the possibility of obstructing the lumen with the consequent manifestations of mechanical ileus. This forms the most frequent complication in both types of bezoars. In trichobezoar this is usually due to the breaking off from the original hair-ball in the stomach of a small portion which so frequently extends through the pylorus and into the duodenum. That this may very likely occur is readily understood by a close examination of these bezoars. For example, in the authors' case the rather long extension into the duodenum was connected to the original trichogenous intragastric mass by a more narrow and less intact area corresponding to the position of the pylorus (Fig. 1). That such small sections do break off is demonstrated by the

fact that not infrequently they are passed in the stools. However, in some instances they become lodged in the intestine, most frequently in the terminal ileum, and then produce the characteristic manifestations of ileus. Of the 156 collected cases, this occurred in 17 (10.8 per cent). As might be expected, this complication is considerably more frequent in phytobezoars, as is shown by the fact that of the 94 collected cases there were 25 (26.5 per cent) with this complication (Graph IX). In our series of 7 cases intestinal obstruction developed in 3 (42.8 per cent). Its greater frequency of occurrence in phytobezoars is due to the fact that they are more likely to be multiple, of harder consistency, and more irregular in surface.

The complications produced by the traumatic influence of these foreign bodies is usually manifested by gastroduodenal ulceration and



Graph IX.—Comparative incidence of complications in bezoars based on 250 collected cases of bezoars, including the cases of DeBakey and Ochsner.

consequent hemorrhage, perforation, and peritonitis. Again, as might be predicted, gastroduodenal ulceration occurs much more frequently in phytobezoars than in trichobezoars. Whereas, of the 156 collected cases of trichobezoars, this complication was present in only 15 (9.6 per cent); of the 94 collected cases of phytobezoars it occurred in 23 (24.4 per cent) (Graph IX). Only 1 (14.2 per cent) of our series of 7 cases had this complication. The most obvious explanation for the higher incidence of gastroduodenal ulceration in phytobezoars is that their harder consistency and more irregular surface have greater potential traumatic influence. Grossly the ulcers complicating bezoars are similar in every respect to peptic ulcers as is illustrated in our case (Fig. 12). Of even greater interest is the characteristic location of these ulcers, which opens a rather intriguing speculative consideration of the etiology of peptic ulcer. Of 10 cases of trichobezoars with ulcers in which the

location was stated, 8 were on the lesser curvature and 2 on the greater. Of the 19 collected cases of phytobezoars including ours, 15 were on the lesser curvature and 4 were on the greater. In our case the ulcer was situated on the greater curvature (Fig. 13). Thus, of the total 29 cases, 23, or approximately 80 per cent, were located on the lesser curvature, an incidence which corresponds fairly closely with that of gastric ulcer. The question which immediately arises is why should ulceration occurring in these cases develop in such a characteristic location and one which corresponds so closely with the site of the ordinary gastric ulcer. It would appear that a foreign body, such as a trichobezoar, forming an almost complete cast of the stomach, should produce an evenly distributed trauma to the mucosa and not a concentrated irritative action to a small area. Moreover, it certainly cannot be con-

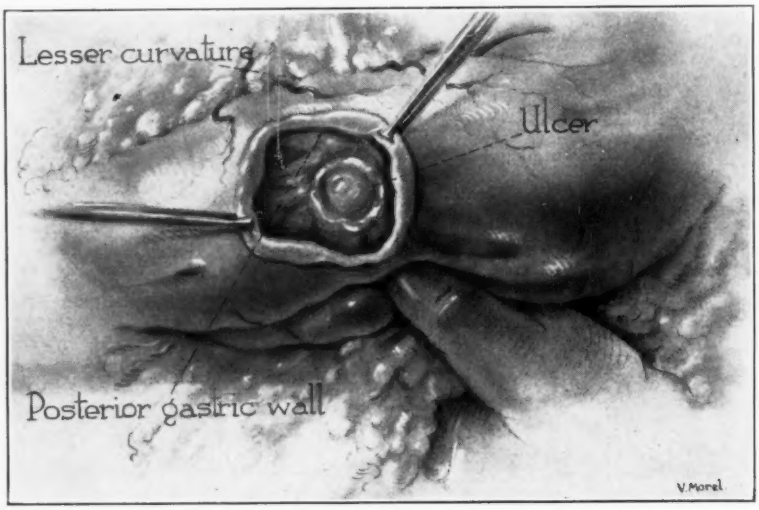


Fig. 12.—Drawing of chronic ulcer along greater curvature of stomach as seen through gastrotomy incision at time of operation as described in Case 7. Grossly this ulcer resembled the ordinary gastric ulcer in every respect.

sidered a coincidence nor can one argue that these individuals would develop ulcers anyway in the absence of bezoar, for the incidence is entirely too high. The occurrence of these ulcers in this strictly limited localization with such striking uniformity almost forces the admission that the mechanism of formation must necessarily closely parallel that of ordinary gastric ulcer. Indeed, it would appear to lend support to the significance of the mechanical factor as propounded by Aschoff,[333] whose conception was based upon a comprehension of the function of the so-called *magenstrasse* or gastric pathway which is assumedly the route by which gastric chyme is propelled from the pylorus into the duodenum. The presence of bezoars further enhances the mechanical or traumatic factor by interference with proper emptying of the stomach, thus creating first, gastric retention which augments and prolongs gastric motility and gastric acid secretion; and second, prevention of

normal duodenal regurgitation which is the major factor in the neutralization of gastric acidity. Furthermore, the characteristic situation of these ulcers would seem to emphasize the significance of tissue susceptibility as a predisposing factor in the genesis of ulcer. That the lesser curvature of the stomach *(magenstrasse)* has an inherent vulnerability or an intrinsic quality of susceptibility to peptic ulceration has been shown by numerous investigators. Morton[334] observed that after "surgical duodenal drainage" procedures, ulcers along the greater curvature healed; whereas, those on the lesser curvature became chronic. This greater sensitivity of the mucosa along the lesser curvature to peptic ulceration has been demonstrated convincingly by Ochsner, Gage, and

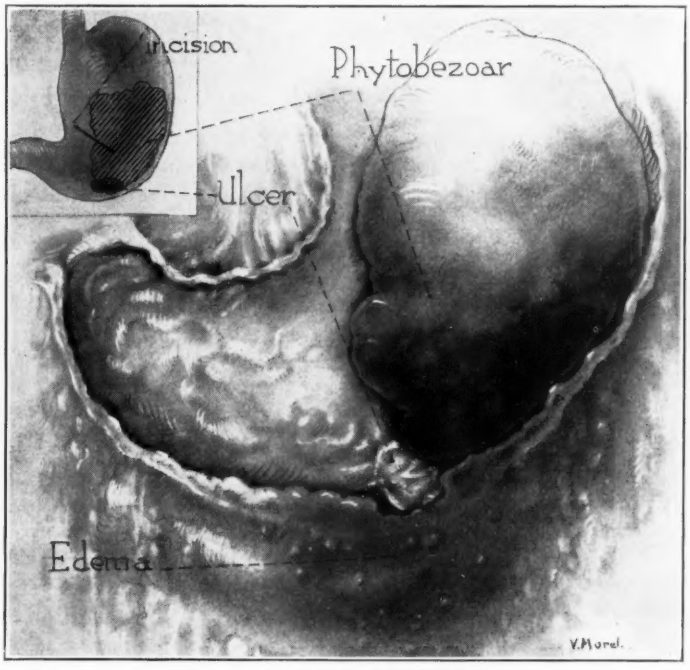


Fig. 13.—Drawing to illustrate relative size of diospyrobezoar removed at operation in Case 7 and to show the relative position of the ulcer along the greater curvature of the stomach.

Hosoi.[335, 336] Thus, the development of these characteristic ulcers in the presence of bezoars may be explained to some extent on the basis of the two factors; namely, tissue susceptibility and mechanical or traumatic.

However, we are fully cognizant of the fact that, whereas these two factors may play the most conspicuous roles in the genesis of these bezoar ulcers, they cannot be considered as the only operating factors. Obviously, if this were true, the incidence of bezoar ulcer would be considerably higher than 15.2 per cent. Moreover, on this basis it would be difficult to explain satisfactorily the absence of ulceration in cases of bezoars existing as long as ten years or more. Undoubtedly, here as in

peptic ulceration in general no single factor can be held solely responsible for their development. A recent recapitulation of the voluminous clinical and experimental investigations clearly indicates that ulcer is the result of a "tesselation of factors."[337] We have expounded previously a thoroughly rational understanding of the physiologic principles involved in the development and maintenance of peptic ulceration and are of the opinion that the occurrence of these bezoar ulcers is not only satisfactorily explained on this basis but even lends support to the exposition.[337-341] This concept maintains that ulcer is established by the summation of two groups of factors: (1) the *predisposing*, which are inherent and therefore uncontrollable; and (2) the *precipitating*, which are controllable. The former group is composed of: (a) tissue susceptibility, which has been alluded to previously and which may be defined as an inherent vulnerability of certain portions of the gastrointestinal tract, such as the lesser curvature of the stomach *(magenstrasse)*, the duodenal cap, etc., to the digestive eroding effect of the acid gastric juice; and (b) constitutional, which is extremely difficult to define and must be considered as an ingrained susceptibility of certain individuals to gastroduodenal ulceration. Whereas the former innate characteristic is present in all individuals, the latter exists only in those individuals who develop ulcer in the presence of the precipitating factors. Thus, both these predisposing factors, i.e., tissue susceptibility and constitutional predisposition, may be present in an individual without peptic ulcer necessarily developing. However, ulceration does occur if to this predisposing group there are added the precipitating factors which consist of (a) chemical, (b) mechanical or traumatic, and (c) infection. On this basis a ready and satisfactory explanation exists for the development of ulcers in that group of bezoar patients having this complication (15.2 per cent) as well as those in which ulcers do not occur (84.7 per cent). The precipitating factor exists in both groups but the constitutional factor is present only in the former. In order for ulcer to develop, both factors must necessarily be present. The fact that the simple removal of the bezoar, or to state it differently, the removal of the precipitating factor, is almost invariably followed by disappearance of the ulcer further corroborates this hypothesis.

These ulcers in bezoars may be complicated further by perforation and peritonitis. Curiously enough, the incidence of perforation in the ulcers of both types of bezoars is about the same. Of the 15 collected cases of trichobezoars with ulcers, 5 (33.3 per cent) perforated and of the 19 collected cases of phytobezoars with ulcers 7 (36.8 per cent) perforated. Whereas death followed all the perforated cases of trichobezoars, this eventuality occurred in only 5 (71.4 per cent) of the phytobezoars (Graph VIII). This may be explained probably by the fact that the intragastric contents of trichobezoars, characteristically foul, are more likely to harbor pathogenic organisms.

Treatment.—The treatment of bezoars and concretions is essentially surgical and consists of the operative removal of the foreign body usually from the stomach and occasionally from the intestines. Conservative measures, consisting of the administration of dilute hydrochloric acid[342] or external massage[189] in an attempt to cause chemical or mechanical disintegration of the foreign body, have been suggested but cannot be approved. Surgical intervention is obviously the only rational therapeutic procedure. This is further corroborated by the self-evident results of the statistical analysis of the collected cases. Thus, whereas the mortality in the nonoperative cases of trichobezoars, diospyrobezoars, and other phytobezoars is 72.7 per cent, 50 per cent, and 66.6 per cent respectively, these corresponding figures in the operative cases are 4.8 per cent, 7.4 per cent, and 4.7 per cent (Graph VII).

It is considered unnecessary as well as inexpedient to attempt here a detailed discussion of the operative technique. However, it is adjudged desirable to direct attention to a few salient technical factors. The type of abdominal incision is of no great moment but should permit an adequate approach to the stomach. Particular emphasis is attached to the care with which intraperitoneal exclusion is done before opening the stomach, especially in trichobezoars. Obviously the gastrotomy incision should be made on the anterior wall and at right angles to the longitudinal axis of the stomach. Because of the frequent enormous size of trichobezoars, it is usually necessary to make a rather large opening in the wall of the stomach. Also, due to the long duration of these intragastric trichogenous masses and the resultant stasis, fermentation, and decomposition, there is usually an associated slimy, foul, putrid material. For this reason special precautions should be taken in the removal of these foreign bodies to prevent possible contamination of a virgin peritoneal cavity. Because frequently there is extension of the hairball through the pylorus and for some distance into the duodenum, the operator should exercise particular care in extracting the entire foreign body.

In considering the operative removal of phytobezoars, it is important to realize the not infrequent concomitant occurrence of two or more intragastric masses as well as the occasional presence of a mass in the intestines. It will be recalled that this occurred in 17.5 per cent and 4.4 per cent respectively of the collected cases of phytobezoars including ours. For this reason a thorough exploration of the stomach is imperative in order to be absolutely certain that all the foreign bodies have been removed. That such a precaution is not stressed unduly is demonstrated clearly by the case of Outten,[190] the case of Davis reported by Hart,[196] and our Case 8. The case reported by Outten, in 1894, is amazingly similar to our Case 8 which was not treated in our service. In both cases there were two intragastric diospyrobezoars. Whereas in Outten's case the second bezoar was recognized and removed through a

second gastrotomy incision before the abdominal wound was closed, in the case reported by us a subsequent operation was necessary. That such a mistake should be repeated forty-four years later is an ironic tribute to medical literary efforts.

Obviously, in the presence of such complications as intestinal obstruction and peritonitis, the institution of appropriate therapy must vary accordingly. The cases of bezoars associated with simple ulcers, i.e., nonperforative, merely require the removal of the foreign body. Because of the pathogenic nature of this type of ulcer, the removal of the traumatic factor usually is sufficient. Our Case 7 readily illustrates this fact. Whereas the ulcer in this case was grossly similar to the ordinary chronic gastric ulcer, following the removal of the diospyrobezoar, which was the traumatic factor, the ulcer apparently healed completely.

CASE REPORTS

CASE 1.—F. L., single, white, servant girl, aged 15 years. Admitted to Charity Hospital Jan. 23, 1935, complaining of vomiting.

For past three months patient has awakened regularly at 2 A.M. to vomit. During this same period of time she has been able to eat only small amounts every two hours. She has experienced slight epigastric discomfort and fullness. Since she began vomiting, she has noticed a large hard mass in upper abdomen. There has been rapid loss of weight recently and considerable weakness. No hematemesis and no constipation.

Patient admitted that as a younger child she used to chew and swallow her hair but at present only bites her nails. However, parents state that during the night while patient is fast asleep, she has been observed to seize her hair, tear it out, and place it into her mouth.

Physical Examination.—Patient is thin and pale. Weight, 82½ pounds. Neuropsychiatric survey "reveals every evidence of an inadequate personality plus a constitutional inferiority. Psychometric study shows middle grade moronity. Neurological examination negative." Temperature, pulse, and respiration normal. Significant findings are in the abdomen only. Inspection reveals a prominence extending from the upper midepigastrium and left hypogastrium diagonally downward to the lower right hypochondriac region. It is displaced downward on deep inspiration and palpable as a well-defined firm mass crescentic in shape, roughly suggesting a dilated stomach. It seems to extend from beneath the left costal margin to a point just below and to the right of the umbilicus. It can be readily moved in all directions. There is slight tenderness but no rigidity.

Laboratory Studies.—Wassermann, negative; urinalysis and blood chemistry, normal; R.B.C. count, 5,290,000; Hb., 75 per cent; W.B.C. count, 12,000; neutrophiles, 86 per cent; small mononuclears, 11 per cent; large mononuclears, 3 per cent. Stool examination: Hair present in feces. Gastric analysis: Free HCl, 4; total acidity, 28. Roentgenographic examination: Fluoroscopic examination following ingestion of barium meal reveals no abnormalities in the esophagus. As the barium enters the fundus, it seems to hesitate and then splits into two layers flowing downward along the greater and lesser curvatures. This defect in the barium shadow is caused by a foreign body as there is no involvement of the walls of the stomach. The six-hour plate shows a greatly distended stomach and duodenum apparently containing a large hairball (Fig. 5).

Preoperative Diagnosis.—Trichobezoar.

Operation, Jan. 31, 1935: Upper right rectus incision. Upon exposing the stomach, it is evident that the tumor is intragastric and completely fills the entire stomach. Further exploration reveals the mass extending through the pylorus into the duodenum. The peritoneal cavity is carefully excluded by packing wet cloths around the exposed anterior wall of the stomach. An incision at right angles to the longitudinal axis of the stomach is made about the middle of its anterior wall. An immense slimy, foul-smelling hairball is found which so completely fills the stomach that it forms a perfect cast of this organ. By careful massage, traction, and manipulation, the mass, which extends into the second portion of the duodenum, is removed in its entirety (Fig. 1). The gastrotomy incision is then closed with three rows of sutures. The wound is closed in layers.

Patient's recovery was uneventful. On March 27, 1935, two months after operation, roentgenographic studies with barium revealed no filling defect in stomach or cap and no six-hour gastric residue. Stomach is normal in size.

Specimen.—Mass consists of firmly matted and closely packed dark brown long hair with a glairy, mucoid surface coating and an extremely foul odor. In contour it resembles a cast of the stomach and part of the duodenum. Particles of fat and other undigested food substances are intimately mixed with the hair. The mass weighs 750 gm. and measures, exclusive of the duodenal extension, 42 cm. along the greater curvature, 21 cm. along the lesser curvature, and 20 cm. in circumference at the fundus (Fig. 1).

CASE 2.—A. M., white, married male, laborer, aged 32 years. Admitted to Charity Hospital, Dec. 20, 1935, complaining of vomiting blood.

Present Illness.—Patient's illness began about one month prior to hospitalization with sudden onset of rather severe cramplike pain during hunger which was relieved following eating. These symptoms recurred every day for two weeks, then he began vomiting small amounts of blood and dark brownish to black material. This continued almost daily until Dec. 20, 1935, the day of admission to hospital, when he suddenly became very weak and vomited a large quantity of blood and passed tarry stools. The cramplike pains have persisted and he has experienced a weighty sensation in the epigastrium. Previously patient had no gastrointestinal disturbances.

Physical Examination.—Patient is thin, obviously in poor health, very weak and pale, apparently almost in shock. Temperature, normal; pulse, 100; and respirations, 28. Significant findings limited to abdomen. No abnormalities observed on inspection. Freely movable firm mass palpable in epigastrium. Slight tenderness but no rigidity present.

Laboratory Examinations.—Wassermann, negative; urinalysis, normal; R.B.C. count, 3,450,000; Hb., 60 per cent.

Roentgenographic examination after barium meal reveals negative shadow in stomach in region of incisura angularis which may be considered as possible polyp. The six-hour plate showed no gastric retention with the meal resting in terminal ileum and cecum.

Because of the secondary anemia, the patient was given two 500 c.c. blood transfusions before operation.

Operation.—Jan. 6, 1936, under ether anesthesia a left paramedian incision is made. Upon examination of the stomach a hard mass about the size of a fist is palpated. The stomach is delivered into the wound and the surrounding area carefully packed with wet cloths. Through a transverse incision made in about the middle of the anterior wall of the stomach a black, hard, oblong-shaped mass about 6 cm. in length and 4 cm. in width is removed. The gastrotomy incision is closed with three rows of sutures. The abdominal incision is closed in layers.

Pathologic Report.—The specimen consists of an oblong-shaped mass firm in consistency and dark brown to black in color, measuring 6½ cm. by 4 cm. by 4 cm. The

external surface is slightly irregular with clefts and pits (Fig. 2). On section the entire inner portion consists of amorphous light brownish material with a dark brownish seed near the center (Fig. 4). Microscopic examination further suggests that this is a phytobezoar, probably of persimmon origin.

The patient was discharged on Jan. 21, 1936, in good condition after an uneventful recovery.

CASE 3.—R. K., white male, electrician helper, aged 25 years. Admitted to Charity Hospital Aug. 12, 1936, complaining of epigastric pain, nausea, and vomiting.

Present Illness.—For several years patient has had vague gastrointestinal disturbances, but during past year condition has become worse rapidly and is manifested by weighty sensation and dull pain in the epigastric region. This is well-localized in character and almost constantly present, although the pain seems to be worse following meals and on assuming different positions. Nothing relieves the pain. During the past few months he has been conscious of a "lump in the stomach." Recently he has become nauseated and occasionally vomits after meals. Appetite is poor and he has lost twenty pounds in six months. No hematemesis or melena.

Past History.—States that when he was 10 to 14 years of age he ate large quantities of persimmons but has not eaten any since.

Physical Examination.—Patient is well-developed but undernourished. Temperature, pulse, and respiration normal. No significant findings except in abdomen.

Inspection of abdomen reveals no abnormalities. On palpation a firm mass about 6 to 8 cm. in diameter is felt in the epigastrium just above and to the left of the umbilicus. It is readily movable from side to side and can be pushed up beneath the left costal margin so that it disappears. It also moves when patient changes position. It does not necessarily move on respiration. There is very slight tenderness and no rigidity.

Laboratory Examinations.—Wassermann, negative; urinalysis and blood studies, normal.

Roentgenographic examination after barium meal: Fluoroscopic examination reveals foreign body in stomach. Gastrointestinal series shows a filling defect of the stomach which has the appearance of a food or hairball (Fig. 6). There is slight six-hour gastric residue.

Preoperative Diagnosis.—Phytobezoar.

Operation, Aug. 13, 1936. Under epidural analgesia, left paramedian incision is made. Upon exposing the stomach, an intragastric freely movable mass, firm in consistency and about the size of a fist, is readily palpable. The stomach with the mass is delivered into the wound and the operative field carefully excluded with wet packs. A transverse incision extending between the greater and lesser curvatures about 6 cm. in length is made in about the midpart of the anterior wall of the stomach. Through this incision by gentle manipulation a firm dark brown to black mass roughly oval to rectangular in shape is removed. The gastrotomy incision is closed with three rows of sutures. The abdomen is closed in layers.

Pathologic Report.—Specimen consists of a firm, hard, dark brownish mass with a slightly fermentative odor measuring 9 by 5 by 2½ cm. The surface is somewhat bosselated with some smooth areas. On section it appears to be composed of an amorphous, yellowish substance which on microscopic examination confirms the diagnosis of phytobezoar probably of persimmon origin.

Patient was discharged on Sept. 24, 1936, in good condition after an uneventful recovery.

CASE 4.—S. F., white, male, aged 10 years. Admitted to Charity Hospital Oct. 10, 1936, complaining of pain in right lower quadrant of abdomen.

Present Illness.—Began suddenly on Oct. 7, 1936, with rather severe colicky pain in right lower abdominal quadrant followed by nausea and vomiting. Had slight

diarrhea at onset but has been constipated since. Patient was given three doses of castor oil but vomited it on each occasion. The nausea, vomiting, and colicky pain have persisted with varying periods of relief. The vomitus is described as being bitter and greenish in color. Also complains of rather severe frontal and temporal headaches. Patient has no appetite and has become very weak since onset of illness. Subsequent questioning of parents reveals that he had engorged himself on persimmons a few days before onset of illness.

Family History.—Parents state that in 1931 an older brother of patient had similar clinical manifestations following ingestion of large quantities of persimmons and was relieved by operation.

Physical Examination.—Patient is well-developed but slightly undernourished, obviously ill, and suffering pain. Temperature, 100° F.; pulse, 120 per minute; and respiration, 36 per minute. Significant findings limited to abdomen which on inspection reveals slight distention. Liver and spleen are not palpable and no masses can be felt. There is moderate generalized tenderness and rigidity most marked in right lower quadrant.

Laboratory Examinations.—Wassermann, negative; urinalysis, normal; W.B.C., 11,700; neutrophiles, 62 per cent; small mononuclears, 28 per cent; large mononuclears, 10 per cent; R.B.C. count, normal.

Diagnosis of intestinal obstruction probably due to phytobezoar of persimmon origin was made. Patient was treated conservatively by phleboclysis of glucose and saline solutions, sedation, and surgical liquids for approximately one week with no evidence of improvement.

Operation, Oct. 18, 1936: Under ether anesthesia a right paramedian incision is made. Upon opening the peritoneal cavity a large quantity of peritoneal fluid escaped. The small bowel is markedly distended. Further exploration reveals a hard round mass in the terminal ileum about 10 cm. from the ileocecal junction which is obviously the site of obstruction. This loop of bowel containing the mass is delivered into the wound and carefully excluded from the peritoneal cavity by packs of wet cloths. A transverse incision is made in the ileum just over the mass and it is readily removed. The mass is dark brown in color, round with an irregular surface measuring about 5 cm. in diameter. The enterostomy opening is closed with three layers of suture. The appendix is examined, found to be acutely inflamed, and removed. The abdominal incision is closed in layers.

The immediate postoperative therapy consisted of: (1) Wangensteen suction, (2) phleboclysis of glucose and saline solutions, (3) heat tent over abdomen, (4) nothing by mouth except water, (5) sedation by morphine gr. ½.

The patient's progress was very satisfactory for four days postoperatively until Oct. 23, 1936, when heat tent and Wangensteen suction were discontinued. At this time ice water, fruit juices, and sweetened soda water drinks were administered. The wound was also observed to be infected and drainage instituted. The following day there was marked abdominal distention; the temperature ranged from 102° to 103° F. and the pulse was 150 per minute. Patient continued to vomit everything given. Enemas were given with no apparent relief of the distention and the patient was obviously getting worse. The heat tent and Wangensteen suction were reapplied on Oct. 27, 1936, but the patient died the following day.

Autopsy.—Oct. 28, 1936: Significant findings limited to peritoneal cavity which contained a large amount of thick purulent yellowish exudate. The loops of bowel are adherent by thin fibrinous adhesions which contain localized collections of pus. Similar collections are above the liver, in the right and left iliac fossae, and in the pelvis. The side of the enterostomy appears intact in the ileum 10 cm. from the ileocecal valve with no evidence of leakage. The site of the appendectomy also reveals no evidence of leakage. The bowel is considerably distended, but there is no evidence of perforation. Within the stomach a round foreign body is found,

dark brown to black in color, measuring 5 cm. in diameter, having an irregular surface, and closely resembling the foreign body previously removed at operation. Subsequent microscopic and macroscopic examinations prove these masses to be phytobezoars containing persimmon seeds. The liver shows evidence of acute hepatitis and perihepatitis and the spleen has the characteristics of acute toxic splenitis. The postmortem diagnosis is: (1) generalized peritonitis, (2) acute intestinal obstruction caused by phytobezoar probably of persimmon origin, (3) subacute appendicitis, (4) acute toxic hepatitis and splenitis.

CASE 5.—Mrs. J. M., white married female, aged 50 years. Admitted to Charity Hospital Nov. 2, 1936, complaining of epigastric pain, nausea, and vomiting.

Present Illness.—Began suddenly on the morning of Oct. 28, 1936, following breakfast with severe cramplike pain in the epigastric region which was followed by marked nausea and vomiting. A physician prescribed castor oil which was repeated before her bowels moved with very little effect. Since then she has been constipated. The nausea and vomiting have persisted. The pain is not as severe, although it has never completely disappeared. She has become moderately distended and weak. The vomitus has recently become foul smelling.

Physical Examination.—Patient is well-developed, rather obese, apparently acutely ill. Temperature, 99° F.; pulse, 100 per minute; respiration, 26 per minute. Significant findings limited to abdomen, which on inspection is moderately distended with no visible masses or scars. The abdominal wall is very thick, making palpatory examination rather difficult. However, no masses could be felt and the liver and spleen are not palpable. There is slight generalized tenderness but no rigidity.

Laboratory Examinations.—Wassermann, negative; urinalysis reveals slight amount of albumin; red cell count is normal; blood culture, negative.

A tentative diagnosis of acute high intestinal obstruction is made, but operation is considered inadvisable because of patient's poor condition. Conservative therapy consists of Wangensteen suction, phleboclysis of glucose and saline solutions, heat tent over abdomen, and morphine sedation. However, patient rapidly became worse the next day and died twenty-four hours after admission.

Autopsy: Nov. 3, 1936: Significant findings limited to peritoneal cavity which contains a small amount of clear straw-colored fluid. The small bowel is markedly distended to a point about 65 cm. from the ileocecal valve below which the bowel appears normal. At this site a foreign body causing the obstruction is found in the lumen of the ileum. It is a firm, black, oblong-shaped, somewhat flattened mass having an irregular surface measuring 4 by 2½ by 2 cm. On section it consists of a light brown amorphous granular substance in which is imbedded a persimmon seed and what appears to be persimmon skin. There are a few vegetable fibers interspersed in the material. Subsequent examination further indicates this to be a phytobezoar of persimmon origin. At the site of obstruction the mucosa seems ulcerated and the bowel is congested and edematous. The liver and spleen present the characteristics of acute toxic hepatitis and splenitis.

Post-mortem diagnosis is: (1) acute intestinal obstruction due to a phytobezoar probably of persimmon origin; (2) acute toxic hepatitis and splenitis.

CASE 6.—A. C., colored male laborer, aged 37 years. Admitted to Charity Hospital Nov. 21, 1936, complaining of "locked bowels."

Present Illness.—On Nov. 16, 1936, five days previous to admission, patient suddenly developed cramplike pain in right lower quadrant. This has persisted with occasional periods of relief, although successive attacks have become more severe. Sometimes the pain radiates down towards the hypogastrium. Bowels have not moved since onset of pain in spite of purgatives. On day before admission immediately following meal he became nauseated and vomited the food ingested. Since then has vomited anything ingested.

Physical Examination.—Patient is fairly well developed but slightly undernourished, apparently dehydrated, and obviously ill. Temperature, pulse, and respiration are normal. Significant findings limited to abdomen which on inspection reveals visible peristalsis. There is moderate degree of distention and enlarged veins are visible over lower abdomen. There is no tenderness or rigidity and no palpable masses.

Laboratory Examinations.—Wassermann, negative; urinalysis: albumin, 3+; few granular casts; blood chemistry: N.P.N., 55 mg. per cent; sugar, 110 mg. per cent; chlorides, 420 mg. per cent.

Roentgenographic examination following barium meal reveals two round tumors approximately 4 to 5 cm. in diameter, one lying in prepyloric region, and the other in the lower portion of fundus of stomach (Fig. 11). They are freely movable in the stomach and have the appearance of bezoars or two pedunculated benign tumors. There is no six-hour gastric residue. Multiple fluid levels are present in the abdomen.

Subsequent questioning of patient revealed that in the fall several months previously he had eaten large quantities of persimmons.

Wangensteen suction applied and 5 per cent glucose and normal saline solutions administered intravenously. On Dec. 5, 1936, patient passed a hard, round mass about 5 cm. in diameter and black in color. Further examination of this mass confirmed the diagnosis of phytobezoar, probably of persimmon origin.

Following this patient began to improve rapidly and left the hospital in apparently good condition on Dec. 16, 1936.

CASE 7.—J. M., white male, aged 59 years. Admitted to Touro Infirmary March 7, 1937, complaining chiefly of pain in stomach. During dinner one evening in January, 1937, about three months previous to admission, he experienced epigastric discomfort and nausea. Previous to this time he had had no gastrointestinal disturbances. Since then, he has had frequent attacks of nausea and cramplike pain in epigastrium. He is often nauseated but rarely vomits. The pain occurs intermittently throughout the day, is relieved sometimes by eating, but is increased about an hour after eating. The pain seems to be generalized over the entire epigastrium and rarely radiates to any other portion of the abdomen.

Past History.—Previously in good health. Patient is a farmer and has persimmon trees in his field. For past three years he has eaten large quantities of persimmons each fall when the fruit ripens. Three years ago when he first began eating persimmons he had some epigastric discomfort and following this for a few days had an attack of diarrhea which he "cured" by drinking oak-bark tea. For a few days following first attack of pain, patient noticed distinct tarry stools, but since then stools have been dark brown in color. Appetite has been good and he has lost very little weight.

Physical Examination.—Patient is well developed, well nourished, and not acutely ill. Temperature, pulse, and respiration are normal. There are no significant findings except in the abdomen.

On inspection of the abdomen no abnormality is observed, but on palpation there is felt a rather firm round mass in the epigastrium. It is about 12 cm. in diameter and is freely movable in all directions, but especially up and down. The mass is frequently "lost" during palpation and seems to recede high in the epigastrium and under the left costal margin. There is slight tenderness, particularly on deep pressure, but no rigidity.

Laboratory Examinations.—R.B.C. count, 4,880,000; Hb., 80 per cent; W.B.C., 12,000; neutrophiles, 70 per cent; small mononuclears, 23 per cent; large mononuclears, 6 per cent; eosinophiles, 1 per cent; gastric analysis: free HCl, 40; total acidity, 60; urinalysis, normal.

Roentgenographic examination after barium meal reveals the barium passing through the esophagus in a normal manner. At the initial swallow of barium, a

large filling defect is seen in the region of the pars media. As the stomach fills, the defect appears to rise toward the fundus of the stomach and the impression gained is that there is a large foreign body within the stomach, either a bezoar or a pedunculated polyp which moves rather freely (Fig. 8). The stomach is very irritable, but at six hours there is a retention of barium, the shadow being very irregular, as though the barium were caught in the meshes of a mass with irregular surfaces. The duodenum appears to be entirely normal and that portion of the meal which has left the stomach is occupying the terminal ileum. At twenty-four hours there are still a number of small flecks of barium in the stomach, apparently adhering to the mass; the remainder is outlining the colon fairly satisfactorily and no lesions are seen.

Preoperative Diagnosis.—Diospyrobezoar.

Operation, March 10, 1937: A left rectus incision is made. Upon examination of the greater curvature of the stomach, in the region of the pars media is an area of edema and induration. The adjacent lymph nodes in the gastrocolic omentum are removed for immediate biopsy study. Upon further examination of the stomach, a large mass is found present in the lumen of the stomach which is freely movable and apparently a foreign body. After excluding the peritoneum and exposing only the anterior wall of the stomach, so as to prevent any spillage, an incision is made on the anterior stomach wall in a transverse direction, in order to expose the interior of the stomach. The foreign body, a phytobezoar, is removed. It is oval and measures 14 cm. in length and 9 cm. in diameter. It has a very dark brownish to black color and in some places is smooth as though it was shellacked, while at other places it is rough and pitted. There are nodular bosselations on the outer aspect. The phytobezoar is removed through the opening in the anterior wall of the stomach and an ulcer found on the greater curvature (Fig. 13). The ulcer is round, about 2½ cm. in diameter, has thickened, over-hanging edges with a dirty granular base (Fig. 12). It is considered that there is no necessity for treating the ulcer, except by removal of the foreign body.

The wound is closed by two rows of suture. The peritoneum is closed in layers with interrupted black silk sutures. The patient made an uneventful recovery.

Pathologic Report.—Tissue specimen measuring 3 mm. by 3 mm. by 1 cm. grossly appears to be a small lymph node surrounded by fat. This is confirmed by microscopic examination and there is no evidence of malignancy. The other specimen is a firm, brownish black oval mass measuring 9 by 14 cm., weighing 460 gm. with a pitted, bosselated surface. On section the internal structure has a light brown to yellow color and seems to consist of an amorphous, somewhat friable material with a few skins and persimmon seeds. Upon drying, the mass shrunk considerably in size, weighing about 60 gm., and crumbled readily. This specimen has all the characteristics of a diospyrobezoar.

The patient made an uneventful recovery. He was observed again and stated that he was completely relieved of all complaints. Roentgenologic studies revealed no evidence of the previous ulcer.

CASE 8.—C. H., colored female, aged 44 years. Admitted to Charity Hospital Jan. 7, 1938, complaining of epigastric pain, nausea, and vomiting.

Present Illness.—Began in October, 1937, following the ingestion of persimmons. Patient lives on a farm and one evening while walking home after working in the fields all day, she passed a persimmon tree loaded with ripe persimmons. She had not eaten anything since breakfast and was very hungry so she stopped and ate over a dozen persimmons to appease her hunger. Following this she became very thirsty and drank a large amount of water from a near-by well. That evening several hours later she experienced rather severe cramplike epigastric pain followed by marked nausea and vomiting and intense diarrhea. This persisted all through the next day but gradually subsided in a few days. She then felt quite well for a few weeks and

then began having dull pain, constant in character and localized to the epigastrium. Occasionally the pain became quite severe and cramplike. She was conscious of a weight sensation in the epigastrium. The pain seemed to have no relation to meals. Nausea and vomiting have gradually occurred more frequently. She is somewhat constipated. She has not vomited or passed blood by rectum. Appetite is poor and she has lost about ten pounds in weight.

Physical Examination.—Patient is somewhat undernourished and not acutely ill. Temperature, pulse, and respiration are normal. Significant findings limited to abdomen, which on palpation reveals a hard mass in the epigastrium just above the umbilicus. It is round and about 7 cm. in diameter. It is freely movable in all directions. There is moderate tenderness but little rigidity.

Laboratory Examination.—Wassermann, negative; urinalysis and blood chemistry, normal; R.B.C. count, 4,050,000; Hb., 90 per cent; W.B.C. count, 7,500; neutrophiles, 70 per cent; eosinophiles, 3 per cent; small mononuclears, 23 per cent; large mononuclears, 4 per cent.

Roentgenographic report following barium meal fluoroscopically describes extensive filling defect in barium shadow without involvement of stomach wall indicative of the presence of an intragastric foreign body (Fig. 10). At end of six hours there is slight amount of gastric retention. At end of twenty-four hours head of meal has reached descending colon, with partial evacuation at end of forty-eight hours.

A preoperative diagnosis of phytobezoar was made.

Operation, Jan. 22, 1938: Under ether anesthesia left upper paramedian incision is made. Exploration of the stomach reveals a hard mass in the prepyloric region. The stomach containing the mass is delivered into the wound and carefully excluded from the peritoneal cavity by wet cloths. A transverse incision is made in about the middle of the anterior wall of the stomach and a black hard round mass about 6 cm. in diameter and having an irregular surface is removed. Subsequent examination proved this mass to be a phytobezoar, probably of persimmon origin. According to the surgeon's recorded dictation, further exploration of the stomach revealed no other masses. The gastrotomy incision was then closed with three rows of sutures. The abdominal incision was closed in layers.

The patient made an uneventful recovery and was discharged on Feb. 1, 1938, in good condition.

On June 12, 1938, she was readmitted to Charity Hospital complaining of nausea, vomiting, and epigastric pain. She stated that, whereas she remained well for about three weeks after her discharge from the hospital in February, 1938, her symptoms gradually returned and at present her complaints are exactly similar to those she had had on her previous admission. Patient has not eaten any persimmons since discharge from hospital. Abdominal examination revealed a hard, irregular-shaped, freely movable mass about 6 cm. in diameter in the epigastrium. There is slight tenderness but no rigidity.

Roentgenographic examination following barium meal revealed a negative shadow filling the distal end of stomach with displacement of barium suggestive of foreign body, probably a bezoar (Fig. 7). At the end of six hours there was 50 per cent gastric retention and at end of twenty-four hours the meal has reached the descending colon, adherent flecks of barium clearly outline the foreign body in the prepyloric region (Fig. 9).

Operation was performed on June 20, 1938, and a firm pyramidal-shaped mass dark brown to black in color having an irregular surface was removed (Fig. 3). On section it was light brown in color, consisting of an amorphous granular material with a persimmon seed in its center. Subsequent examination proved it to be a phytobezoar, probably of persimmon origin.

The patient had an uneventful recovery and was discharged in good condition on July 4, 1938.

Although the surgeon found only one intragastric foreign body at the first operation, a subsequent examination of the preoperative plate shows the presence of two intragastric foreign bodies, one in the pyloric and the other in the fundic ends of the stomach (Fig. 10). This case illustrates the necessity of careful fluoroscopic, radiographic, and operative examinations in all cases of bezoars.

SUMMARY

1. A critical analysis of 171 cases of trichobezoars, 119 cases of phytobezoars, and 13 cases of concretions, collected from the world literature, and a presentation of 1 additional case of trichobezoar and 7 additional cases of phytobezoars or persimmon bezoars form the basis of this communication.

2. A succinct historical résumé of bezoars is given.

3. The several varieties of bezoars are classified into trichobezoars, phytobezoars, trichophytobezoars, and concretions. The trichobezoar consists of a large quantity of hair of varying lengths, firmly matted together, frequently completely filling the stomach, and consequently assuming its shape. The phytobezoar is composed of a variety of vegetable material, including fibers, skins, seeds, leaves, roots, and stems of plants molded together and forming a compact mass. The most common form of phytobezoar is due to the ingestion of persimmons. Of the 126 collected cases of phytobezoars, including ours, 92 (73 per cent) were of this type. Because of this fact and because of its distinctive clinical and physical characteristics, it is considered desirable to separate it from other phytobezoars by a more significant term. For this reason we have suggested the term "diospyrobezoar," from the Greek etymon, *Diospyron* (meaning Jove's grain), which is the generic name for the wild persimmon. The most common form of concretion is due to the imbibition by painters or furniture employees of furniture polish, which consists mainly of a strong alcoholic solution of shellac; the drinking of water after its ingestion precipitates the resin into an accumulated mass.

4. Of 142 collected cases of trichobezoars, including ours, in which the age was determined, over 80 per cent occurred *before* the age of 30 years. Of 90 collected cases of phytobezoars, including ours, in which the age was determined, over 70 per cent occurred *after* the age of 30 years.

5. Of 152 collected cases of trichobezoars, including ours, in which the sex was determined, there were 139 (91.4 per cent) females and 13 (8.5 per cent) males. Of 96 collected cases of phytobezoars, including ours, there were 22 (23 per cent) females, and 74 (77 per cent) males.

6. Whereas only 9 per cent of the collected cases of trichobezoars demonstrated some psychic or mental disturbance, trichophagia is considered a "personality maladjustment" and patients exhibiting this

characteristic are believed to have some underlying neurologic or psychiatric disturbance.

7. In discussing the development of phytobezoars, it is necessary to consider them under two groups: (1) diospyrobezoars, resulting from the ingestion of persimmons; and (2) other phytobezoars, due to the ingestion of a variety of other vegetable and plant matter. The mechanism of formation of the former is essentially chemical and depends upon the presence of soluble shibuol, a phlobatannin, which under the influence of gastric juice becomes transformed into a sticky coagulum cementing into a ball pieces of skin and seeds which may be present. On the other hand, the mechanism of formation of other phytobezoars is essentially mechanical and depends upon the insoluble and indigestible fiber content.

8. The characteristic clinical manifestations of trichobezoar are a rather large, firm, freely movable epigastric mass, associated with some pain, nausea and vomiting, anorexia, weakness, and loss of weight. In a series of 131 collected cases of trichobezoars, including ours, an abdominal mass was present in 115 (87.7 per cent); abdominal pain occurred in 92 (70.2 per cent); nausea and vomiting, in 85 (64.9 per cent); weakness and loss of weight, in 50 (38.1 per cent); and constipation and diarrhea, in 42 (32 per cent). Of 94 collected cases of phytobezoars, including ours, these clinical manifestations occurred in 54 (57.4 per cent), 80 (85.1 per cent), 70 (74.4 per cent), 31 (32.9 per cent), and 30 (31.9 per cent), respectively.

9. A slight secondary anemia and a mild leucocytosis are usually observed in cases of bezoars. Gastric analysis in trichobezoars may reveal strands of hair and usually a normal or low acidity. Gastric analysis in phytobezoars usually reveals a normal or hyperacidity.

10. Roentgenographic examination, especially after the ingestion of a barium meal, reveals characteristic findings and almost invariably demonstrates the intragastric nature of these foreign bodies.

11. The prognosis in bezoars depends primarily on the presence or absence of two factors: (1) the institution of adequate therapy and (2) complications. The mortality in the nonoperative collected cases of trichobezoars, diospyrobezoars, and other phytobezoars is 72.7 per cent, 50 per cent, and 66.6 per cent respectively in contrast to the corresponding incidences in the operative cases of 4.8 per cent, 7.4 per cent, and 4.7 per cent respectively. Whereas the mortality in the collected cases of trichobezoars and phytobezoars with complications is 53.1 per cent and 18.7 per cent respectively in those cases without complications, these corresponding figures are 10.4 per cent and 2.1 per cent.

12. The total mortality in the collected cases of trichobezoars, diospyrobezoars, and phytobezoars, including ours, was 19.1 per cent, 9.8 per cent, and 12.5 per cent respectively.

13. The complications resulting from the various types of bezoars are due primarily to: (1) interference with the normal physiologic activity of the gastrointestinal tract; namely, obstruction and exhaustion or inanition; and (2) traumatic irritation to the stomach and bowel wall and its consequences; i.e., mucosal erosion, ulceration, perforation, and peritonitis. Of the collected cases of trichobezoars, intestinal obstruction occurred in 10.8 per cent, gastroduodenal ulceration in 9.6 per cent, perforation of ulcer in 3.2 per cent, peritonitis in 3.8 per cent, and exhaustion in 8.3 per cent. These corresponding incidences in the collected cases of phytobezoars, including ours, were 26.5 per cent, 24.4 per cent, 7.4 per cent, 8.4 per cent, and 1 per cent.

14. Of the collected cases of trichobezoars complicated by peritonitis, perforated ulcer, gastroduodenal ulcer, and intestinal obstruction, the respective mortality incidences were 100 per cent, 100 per cent, 53.3 per cent, and 47 per cent. The corresponding incidences in the collected cases of phytobezoars were 75 per cent, 71.4 per cent, 21.7 per cent, and 16 per cent.

15. The treatment of bezoars and concretions is essentially surgical and consists of the operative removal of the foreign body, usually from the stomach and occasionally from the intestines.

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